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PAPERS OF A SEMINAR ON EARLY WARNING SYSTEMS FOR TOXIC SUBSTANCES

Benigna Carroll

Battelle Memorial Institute

Prepared for:

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National Institute of Environmental Health Sciences
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PAPERS OF A SEMINAR
ON
EARLY WARNING SYSTEMS
FOR TOXIC SUBSTANCES

CONFERENCE REPORT

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necessarily reflect the positions of
those sponsoring organizations.

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FOREWORD

These proceedings present the results of a 3-day seminar held at Battelle's Seattle Research Center early in 1974. The purpose of the seminar was to examine some of the tools that currently exist which may be applicable to the early identification, assessment and prioritization of chemical substances that impact adversely on man or his environment. The need for early warning tools is clearly evident when one considers (1) the large number of chemicals to which people are exposed in their daily lives and (2) the well-publicized incidences involving such chemical substances as mercury, thalidomide, polychlorinated biphenyls, and, most recently, vinyl chlorides. In principle, there are two or three points in the lifespan of a chemical where early identification of potential hazards can be attempted. For new substances this would be at a reasonably early point in the laboratory pilot scale-commercialization sequence. For substances already commercialized and in use, identification before the level of usage increases significantly or the substance is incorporated into a new product line or use category is desirable. In each case, one is faced with the problem of identifying candidate substances and deciding which among them present the more significant hazard so that the allocation of limited resources for their study and control can be made.

Many institutions face a similar problem of early identification of problem substances, although usually the domain of concern is a relatively narrow one. For example, NIOSH focuses on the work place, NCI on carcinogens, etc.

Participants in this seminar were invited from a cross section of organizations concerned with early warning systems. Thus, representation was a mixture of U. S. government agencies, industry, research institutes, universities, Canadian government agencies, and a public-interest group. Names of the participants are appended to the proceedings.

Not all the speakers provided written papers. Where possible, abstracts of missing papers are included. The papers submitted are arranged in the order of their delivery at the seminar. A detailed seminar program is also appended.

While no solutions to the problem of identification before-the-fact of toxic substances was arrived at, or even expected, a number of issues regarding the need for, workability and practicality of, early warning were raised. Continued examination of the subject would be desirable.

James E. Flinn*
Arthur A. Levin**

SEMINAR

ON

EARLY WARNING SYSTEMS FOR TOXIC SUBSTANCES

Cosponsored by

BATTELLE MEMORIAL INSTITUTE
ENVIRONMENTAL PROTECTION AGENCY–
OFFICE OF TOXIC SUBSTANCES
NATIONAL INSTITUTE OF ENVIRONMENTAL HEALTH SCIENCES
NATIONAL SCIENCE FOUNDATION

January 30 – February 1, 1974

BATTELLE'S SEATTLE RESEARCH CENTER
4000 Northeast 41st Street
Seattle, Washington 98105

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PROGRAM

Tuesday – January 29, 1974

7:00- 9:00 Registration and Mixer at the Center

Wednesday – January 30, 1974

8:30- 9:00 Registration at the Center

9:00 Welcome, T.W. Ambrose, Battelle's Seattle Research Center

9:05 Introductory Remarks, Mr. Frank Butrico, Battelle Memorial Institute

9:15 Keynote, Dr. Norton Nelson, New York University Medical Center

SESSION I EFFECTS, LEGISLATION, AND INCIDENTS

Chairman Farley Fisher, Office of Toxic Substances, Environmental Protection Agency

9:45 Session Chairman's Comments

9:50 Human Health Aspects – Anthony Colucci and Paul Brubaker, NERC-Research Triangle Park, Environmental Protection Agency

10:20 Coffee Break

10:50 Environmental Aspects – John Fortesque, Brock University, Canada

11:20 Legislation and Laws – Michael B. Brownlee, U.S. Senate Commerce Committee Staff

12:00 LUNCH

1:00 An Incident of Industrially Related Toxic Peripheral Neuropathy–Bobby F. Craft, National Institute of Occupational Safety and Health

1:30 An Industry's Experience – Elmer P. Wheeler, Monsanto Company

2:00 Coffee Break

2:20 Panel Discussion on Institutional Perspectives of Early Warning–Chairman Otto Bessey, National Institute of Environmental Health Sciences

Thursday – January 31, 1974

SESSION II EARLY WARNING SYSTEM ELEMENTS

Chairman Ronald S. Goor, National Science Foundation

9:00 Session Chairman's Comments

9:05 General System Requirements–Benigna S. Carroll, Environmental Protection Agency

9:35 Establishing Priorities for Synthetic Organic Chemicals–Philip H. Howard, Syracuse University Research Corporation

10:05 Proposed International Registry on Potentially Toxic Chemicals—Cyrus Levinthal, Columbia University

10:35 Coffee Break

10:55 Model Ecosystems and Toxic Substances—Robert L. Metcalf, University of Illinois

11:25 Anticipating Hazards of Low Level Exposure to Toxic Substances—Cyrus Levinthal, Columbia University

11:55 Methods for Detection of Teratogenic Agents—Thomas H. Shepard, A. Fantel, T. Regimbal, University of Washington

12:30 LUNCH

1:30 Environmental Health Criteria and Monitoring Programs of the World Health Organization—F. Gordon Hueter, Environmental Protection Agency

2:00 Should Assessment Include Cost-Benefit Tradeoffs—Dennis P. Tihansky and Harold V. Kibby, Environmental Protection Agency

2:30 Problems with Early Warning Systems for Toxic Materials—W. Fulkerson, Oak Ridge National Laboratories

3:00 Coffee Break

3:20 Panel Discussion on Early Warning System Elements—Chairman John L. Buckley, Environmental Protection Agency

5:30 SOCIAL HOUR

6:30 BANQUET—Speaker, Glenn L. Schweitzer, Director, Office of Toxic Substances, Environmental Protection Agency

Friday — February 1, 1974

SESSION III EARLY WARNING SYSTEMS/SUBSYSTEMS
Chairman James E. Flinn, Battelle's Columbus Laboratories

9:00 Session Chairman's Comments

9:05 Review of Health/Environment Systems with Potential Early Warning Applications—Theodore J. Thomas and James E. Flinn, Battelle's Columbus Laboratories

9:35 Program to Acquire and Analyze Information on Chemicals Impacting Man and Environment—Arthur A. McGee and Kirtland E. McCaleb, Stanford Research Institute

10:05 NCI Program of Cancer Surveillance, Epidemiology, and End Results Reporting (SEER Program)—James E. Murray, National Cancer Institute, Department of Health, Education, and Welfare

10:35 Coffee Break

10:55	Environmental Impact of Chemicals—Robert J. Moolenaar, Dow Chemical Company
11:25	Environmental Stressor Matrix System for Early Warning—David L. Morrison, Battelle's Columbus Laboratories
11:55	Public Interest Methods for Assessing Chemicals—Albert Fritsch, Center for Science in the Public Interest
12:30	LUNCH
1:30	Panel Discussion on the Concept of Early Warning, Existing Systems, Research Needs, and Implementation—Chairman David L. Morrison, Battelle's Columbus Laboratories
4:00	ADJOURN

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EARLY WARNING SYSTEMS FOR TOXIC SUBSTANCES

January 30 - February 1, 1974

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INTRODUCTORY REMARKS

Frank A. Butrico
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It has long been recognized that decision makers need information to evaluate the present and potential hazards of environmental contaminants, and to have this information in advance of a problem becoming a crisis. Also, it is becoming evident that decisions made in reaction to a crisis are less effective.

In these opening remarks, may I share with you some background information.

My first exposure to the need for early warning was back in 1960 when the Environmental Sciences and Engineering Study Section at NIH planned a conference on the physiological aspects of water quality. The basic concept of the conference was to delineate the physiological and toxicological factors of chemical constituents in water. The conference examined the significance of trace minerals and what were referred to as exotic chemical substances in water supplies, and cancerous hazards that may be associated with natural and artificial water pollutants.

The summary of the conference included the following observations:

> "One of the reasons for calling this conference was to examine research needs and consider what should be done in the future. The needs include not only specific research projects, but questions of surveys or reorientation, and legislative programs"

The summarizer continued:

> "It seems to me one of the papers pointed out that a survey program, based on analytical determinations directed toward specific safety questions and dealing with specific organic contaminants, has much greater value than one directed to the determination of organics in general or to classes of compounds. It is rather generally true, and I think this has become evident in the session on organics,

that you cannot judge the physiological effect solely on the basis of the class of compounds to which a chemical belongs. This applies whether one is concerned with carcinogens or other kinds of toxicity. Accordingly, there must be a close orientation and integration between the survey program and the physiological studies."

The person who made those statements in 1960 is our keynote speaker - Dr. Norton Nelson.

The next event I would like to mention is my contact with the program officer of the then National Environmental Health Sciences Center. To put it simply and bluntly, top management of NEHSC was somewhat embarrassed in not having data with which to answer questions from the "Hill" about problems which were appearing in the press and journals. Staff were asked to take steps to develop some methodology for flagging these potential problems in advance. The result was a study undertaken by Battelle to develop a system to maintain an active overview of chemical contaminants as they move in the market-place. To test out the system, we were asked to examine (in a retrospective sort of way) the contamination potentials of mercury, vanadium, nickel, fluorocarbons, and pulp and paper production. This was a preliminary cut and was not followed up. I would like to point out two significant aspects of this study. One of the problem areas we studied was mercury. The data pointed out that significant amounts of mercury were being "lost" in the environment and, as a result, mercury residue contamination could be expected to be found in food and water. Although this observation was made in 1967, mercury contamination was not considered seriously until at least 3 years later, when residues were detected throughout the U. S. and Canada. Thus, early-warning systems are useless if they go unheeded.

Secondly, we made available some data in the "system" on thalidomide to some toxicologists, and it was their conclusion that if this information had been examined by some astute toxicologists, it might have been possible to identify the thalidomide problem 2 years in advance of its having been removed from the market.

The closest to a follow-up to this study was one made for the Consumer Protection and Environmental Health Service. In this case, the person concerned with the CEPHS R&D effort was faced with the problem of establishing some mechanism for setting priorities among problem areas in order to better allocate limited R&D funds among the various categorical programs. Dr. Morrison will be talking more about this later.

There are two other early-warning-type activities worthy of mention. One is the National Environmental Protection Act (NEPA). In my opinion, this effort to look at environmental impact of projects has been only partially successful. On the positive side, it has forced something to be done but, on the negative side, not all assessments are being taken seriously, so that the effectiveness of the results is questionable. Another factor is that conservationists have been initiating what, in my opinion, have been unrealistic legal actions which are forcing court rulings that may tend to weaken the Act.

Another is technology assessment. For about 5 years, there has been a great deal of attention focused on this subject, culminating in the passage of Public Law 92-484, setting up a Technology Assessment Office, which is just getting under way. The verbiage which preceded passage of the Act is interesting, in that it gives some indications how some people view technology assessment. It is looked upon as:

> "... a mixture of early-warning signals and visions of opportunity."

> "... scrutinizing the interactions, side effects, byproducts, spillovers and tradeoffs among several developing technologies or between a new technology and society at large and the environment."

> "... a device for winning public acceptance of technological change and for improving the quality of information available to decision makers."

> "... a means by which information now available can be used to increase the perception, foresight, and wisdom of decision makers rather than a process for decision optimization."

> "... a first fumbling attempt by members of the scientific meritocracy to engage themselves in the political process, and unreal search for metaphysical values, or merely a device for shaking up the status quo."

> "... the need for some type of early warning device which would trigger a systematic and deliberate evaluation of both the benefits and costs of technological change."

What actually will be done, only time will tell.

With regard to this symposium, I do believe there is an opportunity to lay the groundwork for an early-warning-type system which may help further past efforts and provide guidance to clarify goals and objectives of related activities being undertaken through NEPA and, soon, the Technology Assessment Office. Also, not to be forgotten, are the provisions of the Toxic Substances legislation pending in the Congress, which will require EPA to publish a list of chemicals that may be dangerous to "health or environment".

Lastly, to be effective, the results of any symposium or conference must have some credibility with the scientific community. I am sure this will be no problem, considering the caliber of the speakers on the program and, most important, the fact that the symposium is cosponsored by EPA, NSF, and NIEHS.

EARLY-WARNING SYSTEM FOR TOXIC SUBSTANCES: HUMAN HEALTH ASPECTS

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ABSTRACT

The design of any early-warning testing system to assess the effects of environmental pollutants on living systems should have as one of its primary goals, studies of the human health effects. This goal has been approached from many directions and is the subject of continuing research and controversy.

Studies in humans are the most difficult to perform not only because of the obvious ethical and legal problems, but also because as a group human populations are more heterogenous, mobile, and behaviorly complex. Clearly, what is needed in any early warning system aimed at assessment of impact on human health, is a multidisciplinary approach encompassing clinical medicine and epidemiology supported by adequate environmental monitoring, biochemical, and physiological research programs.

This discussion will focus on the current state of the art in each of these areas and suggest, based on previous results, the utility of such an approach as well as suggestions for its further development.

This topic of discussion includes those programs within EPA such as: Community Health and Environmental Surveillance System (CHESS), Clinical Laboratory Evaluation and Assessment of Noxious Substances (CLEANS), Assessment of Cellular Toxicity and Interactions of Noxious Substances (ACTIONS), Community Pesticide Studies, National Environmental Banking System (NEBS), and the programs of Department of Health, Education and Welfare (DHEW), National Institute of Occupational Safety and Health (NIOSH), National Institute of Environmental Health Sciences (NIEHS), Food and Drug Administration (FDA), and other groups as well.

PRELIMINARY CONSIDERATIONS

There are a few preliminary considerations regarding national health that need to be addressed prior to addressing the human health aspects of an early-warning system relative to toxic substances. A few selected indices of the health status of the American public are not only alarming but aid in placing the magnitude and scope of early warning systems in perspective. Consider the following comments that can be found not only in the lay press but scientific literature as well. The life expectance of our American male population has not substantially increased since 1948. There are 26 million Americans suffering from malnutrition who constitute a rather large segment of the population which is more susceptible to enhanced environmental stress. Other susceptible subgroups of the population that are not included in this figure are children and those people predisposed by preexisting overt illness, age, pregnancy and genetic deficiencies. In accord with fundamental biological laws and theories, a deteriorating environment influences the reproductive capability of a given species. There were approximately 22 infant fatalities per 1000 live births during 1970 alone. Furthermore, estimates indicate that one out of every 130 conceptions ends before the female realizes she is pregnant. Approximately, 25 percent of all conceptions fail to reach an age such that they can survive the womb. In addition, it is important to realize that 5 out of every 100 live births are handicapped by genetic anomalies. The question regarding the significance of these considerations can be partially evaluated by inspecting the number of hospitals, available hospital beds, the number of patients admitted and operating cost expended. In 1947 there were 6173 hospitals with 1.4 million beds that admitted 17.8 million patients. In 20 years the number of hospitals has increased by 15.6 percent and the number of beds by 21.4 percent while the number of patients rose 68.0 percent. In the same time frame, annual operating costs increased 693 percent from 2.4 billion (132.35/patient) to 19 billion dollars ($638.3/patient). This cost analysis does not consider losses from the work force and manufacturing output, the impact of permanent disabilities subsidized by medicare programs, inflationary adjustments, or population modes.

Mortality and longevity are important considerations in evaluating population vitality. At the present time American male longevity ranks 17th among the nations of the world, infant mortality, 16th; while fetal death stands at 24th.

It is perhaps an understatement with respect to the above considerations to stress the need for an early-warning system. However, it is of primary importance to clearly state the objective of such a system; to consider the success of various preventative medical procedures that have addressed the objective, and to evaluate these systems with specific consideration given to the environmental substances.

OBJECTIVES OF EARLY-WARNING SYSTEM FROM HUMAN HEALTH VIEWPOINT

In terms of human health, the principal objective of an early-warning system is to detect asymptomatic, preclinical disorders, as well as overt diseases, in early stages of subacute pathogenesis, and to promote environmental and medical management of associated factors in order to prevent the onset of acute pathology requiring hospital care. Further, attention must be given to the definition of health and essential factors required to accomplish this objective. Health, as defined by the World Health Organization, is a state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity. In order to accomplish the objective, effort must be made to separate the healthy from the unhealthy, to diagnose the observed disorders and to have confirmative follow-up examinations with subsequent treatment in order to reduce hospital admissions and hospital residence time. In order to maintain an effective prevention program, the etiology of the disorder must be addressed with appropriate environmental monitoring, sustained periodic medical examinations, and epidemiology with continued refinement of existing procedures through aligned integrated toxicological and clinical research programs.

Screening is the systematic evaluation of a population to distinguish healthy from unhealthy individuals. To be specific, it is the presumptive identification of unrecognized early disease states through application tests and examinations. It is an aspect of chronic disease control without which diagnosis, follow-up examinations, and treatment become wasteful expenditures of valuable medical-care resources. In recent years a number of multiphasic screening techniques have been employed by a number of federal, state, and industrial organizations.

Let us review several of these systems currently in existence and discuss their present utility as well as how they can be incorporated into an effective early-warning system.

Epidemiological and clinical studies in both Government and industry, such as EPA-CHESS (Community Health and Environmental Surveillance System) and Community Pesticides Studies, CLEANS (Clinical Laboratory Evaluation and Assessment of Noxious Substances), NIOSH (National Institute of Occupational Safety and Health), AEC (Atomic Energy Commission), have many factors in common. These programs are a combination of environmental monitoring for toxic materials and studies of morbidity and mortality patterns in exposed populations at large and in human volunteer groups. Currently these programs are used to predict changes in trends of existing pollutants, but they could be expanded into an early warning system by broadening the scope of pollutant monitoring and exposure and by improving health information gathering.

Examples of improvements in health-information gathering include development of biochemical, physiological, and behavioral indicators that could be measured in populations and would indicate early preclinical disorders Examples of such systems currently being developed include:

1. The use of gas chromatographic analysis of urine specimens to detect metabolites of potentially harmful compounds such as organophosphorus pesticides, etc.

2. The use of gas chromatographic analysis of urine to detect changes in the profile of metabolites which are controlled by liver microsomes.

3. The use of selected blood and urine enzymes which are not pollutant specific but which predict early changes in critical organ metabolism. Example: ornithine-citruline, glutaryl transcarbamylase, serum glutamic oxaloacetic transaminare, alkaline phosphotase.

4. The use of placental enzyme activity profiles to indicate possible pollutant stress on both mother and fetus and thus serve as an early warning of possible predisposition to disease. These enzymes can be more pollutant specific, for example, palmityl transferase, sulfitase, isocitric dehydrogenase, G-6P dehydrogenase or pollutant specific enzymes such as BaP hydroxylase, superoxide dismutase, and carbonic anhydrase.

5. The use of human leucocyte enzyme systems to predict early changes in biochemical parameters such as

nucleic acid synthesis, fatty acid metabolism, glucose metabolism, protein synthesis, along with cytologic changes such as chromosomal aberrations, etc.

6. The use of changes in endogenous antioxidants such as Vitamins E and C to detect early damage by oxidizing compounds such as nitrogen dioxide and ozone.

7. Studies of pulmonary function using field spirometric techniques.

8. Studies of the growth of lung function in children.

9. Studies of changes in tolerance to work stress in patients with known cardiac disorders.

10. Studies of EEG and behavioral changes in response to pollutant stress. One example of this is the appearance of these changes induced by carbamates prior to its detection in the blood.

11. Changes in reproductive patterns in human populations.

One prototype of an early-warning system is the integrated system being developed by the Kaiser Permente Program currently operative in five western states. This system employs an average of 15 basic procedures. Initially an individual is registered and information is obtained regarding his environment. An appointment is then scheduled for the remainder of the study that encompasses nearly a three-hour period. Physiological, psychological, chemical-biochemical and socioeconomic data are gathered, submitted to computers for organization, reduction and summary reports. Electrocardiographic, chest X-rays, blood pressure, pulse rate, visual acuity, hearing, lung function, height, weight, etc., are among the various testing parameters employed. All women over 47 undergo mammiographic studies for cancer. Blood and urine samples are taken from each individual for 17 routine clinical tests processed by automated chemical analyzers to assess levels of normal body chemicals (e.g., protein, cholesterol, uric acid, and calcium). White blood cell, hemoglobin, rheumatic factor, and venereal disease analysis are also performed on collected blood samples. Following completion of these procedures each individual is given a self-administered medical and psychological questionnaire containing 360 items designed to provide some information pertaining to the biological and psychological factors associated with human health with indirect information regarding the individual's environment. In 1969 the cost of this service was $21.32 per individual excluding physician and paramedical services. At this point it is important to realize that a screening program is only the laboratory facet of the complete health analysis. Identical results on two individuals can mean differences in diagnostic procedure due to individual variation in physiology. Therefore, it is important to realize the distinction between screening and diagnosis, that can only be done by physicians, requires other remaining relevant information. In other words, apart from individual biological or physiological variation, people are human beings, each with unique social, psychological and cultural imperatives that are important and often determining factors in their state of health.

There are some primary important considerations relevant to the successful operation of such a screening program. Among these are public relations management, facility location, margin of error, nutritional status and variation, reliability of screening methods and equipment, progressive obsolescence in existing instruments, procedures and protocols. In existing systems over 50 percent of the individuals screened are going to be unnecessarily frightened by false positives. Increased financial burden is enhanced through subsequent evaluation of these false positives as well as false negatives that later appear as hospital admissions. There are a variety of error sources in multiphasic automated screening programs as outlined above. Statistical considerations alone provide some insight in probabilities and confidence limits. If normal limits are defined by the central 95 percent of the results obtained, the probability that a normal individual will be abnormal on any one determination is 0.05 or one in 20. If 12 different determinations are made on a normal individual or the probability of having all of the tests fall in the normal range is 0.95, only 54 percent of a healthy population would have a completely normal profile. Therefore, as the number of tests increases, the probability of false positives increases. Furthermore, it must be remembered that an abnormal result is not synonymous with disease or impending pathology.

Imposed upon these factors is the fact that most of the laboratory and other data on human physiology comes from a rather sparse population of healthy individuals that have volunteered to undergo examination, i.e., medical students, military personnel, prison inmates, etc. Other data on human physiology is derived from the case histories and bodies of sick people. It must also be realized that except for incidence of certain communicable diseases that must be reported, the health records of all private and public hospital patients are private and confidential. Therefore, access to relevant information can be a problem. There are means of obtaining information through appropriate legal caveats by various epidemiological programs. However, inspection of birth and death certificates are often vague and of little use in evaluating population health trends.

Despite these problem areas there has been successful research using multiphasic screening techniques. In 1965 the annual hospitalization admission rate for Northern California members of the Kaiser health program was 80 admissions per 1000 members while the national level was 137.9 per 1000 people. Residence time in hospitals was reduced by half: 532 days for Kaiser Plan members as compared to 1061 days per 1000 sick people as a national level. This impressive record was accomplished largely without the use of automated electronic hardware. Since 1964, the Kaiser centers have introduced automated clinical chemistry instrumentation and data processing equipment. Needless to say, the impact of automation, while initially expensive, refines the efficiency of data collection processing concomitant with reduced paramedical personnel. The use of automated clinical laboratory test procedures has been successful not only in the United States but in other countries as well. In Canada, the results of 32 tests on body-fluid samples obtained from 1010 randomly selected volunteer outpatients indicated some 430 individuals with unexpected abnormal results, notably, within statistical probability. Upon further consultation, 253 of these individuals declined further examination and testing; only 95 of the remaining 177 agreed and actually participated in follow-up examination. The result of the follow-up exams revealed 28 percent of the 95 with subclinical disorders that include diabetes, urinary-tract anomalies, and liver, lung, thyroid, and blood disorders. In Sweden, 35 chemical laboratory determinations performed on 995 apparently healthy randomly selected 45-65 year old individuals revealed a 30.4 percent incidence of disorders ranging from cancer to bacteruria in males with a 53.0 percent incidence in women. The net result of mechanization is the obvious impact on cost in that many tests can be done for the price of a few. Furthermore, professional time, retesting frequency, and unnecessary treatment tends to be minimized with reduced patient anxiety. All of these studies indicate that early warning systems of this type are useful and can be applied in a practical manner.

Emerging on the horizon is still another system which should prove most useful as an early-warning system. Reference is made to the NEBS (National Environmental Banking System) which this year is getting under way through the cooperative efforts of the Environmental Protection Agency, National Science Foundation, Oak Ridge National

Laboratory, and National Bureau of Standards. In addition since Japan, Sweden, Belgium, and Spain have agreed to participate, the NEBS will hopefully be global in scope. In this system samples of tissue from humans and other biota along with specimens of environmental media such as air, water, soil and food will be preserved, stored, cataloged and selectively analyzed for pollutants.

The system will not only provide flashback capability in the event new problems emerge, but will also provide a predictive function by having a broad scope of chemical analyses with documented changes in accumulation of potentially harmful pollutants that can be used to detect problems very early and forecast future problem areas.

Another area of need is the development of rapid in vitro screening systems for toxic substances which are more predictive than present systems and have valid extrapolatability to man. We would not attempt to review the myriad types of systems which have been proposed to date but it can be safely said that each has its own inadequacies. These inadequacies stem largely from the obvious difficulty in extrapolation of animal data to man compounded by the jump from all isolated preparation to any in vivo system.

Still, if we will pay the price, these systems can be constructed and ultimately give credibility and legal sanction. Unfortunately no one group or combination of groups has had the unique insight or resources to pursue in a logical progression enough compounds from in vitro to in vivo mouse and man to establish a predictive system.

Future attention must be focused in this area of need and emphasis placed on the chemical structure biological activity relationship throughout. Clearly not every potentially harmful compound can be screened. Therefore a body of knowledge regarding toxicity of chemical structures has to be accumulated. To date such information is accumulated either in retrospect (as with drugs) or by chance (such as with chlorinated hydrocarbons) but this approach will not suffice for the future.

In conclusion, it should be stated that what we have presented is only a brief overview of the current state of the art and we are sure many programs have not been discussed. Similarly, no attempt was made to outline the myriad needs in environmental monitoring and analysis upon which any early-warning system depends. Hopefully, throughout this conference, all these needs will be addressed and readdressed such that a new program with new approaches will emerge based on collective mutual interest and begin to solidify into a useful early-warning system for toxic substances.

LANDSCAPE GEOCHEMISTRY AND ENVIRONMENTAL PROBLEMS

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ABSTRACT

Geochemistry is a scientific discipline which is concerned with the role of all elements in the synthesis and decomposition of natural materials located at, or near, the daylight surface of the Earth. Landscape Geochemistry is that part of geochemistry concerned with the synthesis and decomposition of natural materials as a result of the interaction of the Lithosphere with the Hydrosphere, Atmosphere and Biosphere. The need for a holistic approach to the design of "Early-Warning Systems for Toxic Substances" is often expressed and the purpose of this paper is to relate this need to research already completed in the fundamental and applied aspects of the Landscape Geochemistry approach. Five examples of research projects of this type will be described briefly and at the end of the paper some conclusions will be drawn regarding the feasibility of the approach in relation to the theme of the seminar.

INTRODUCTION

Our topic today is early-warning systems for toxic substances which have been added to the environment. From the viewpoint of geochemistry the addition of such substances to the environment is essentially an act which modifies the natural circulation of chemical substances between the different components of the systems which occur at, or near, the daylight surface of the Earth. The geochemist stresses the natural circulation patterns of elements which can be used as a basis for the detection of imbalances harmful to man caused by the short, or long, term application of toxic substances to the environment.

In order to stress the holistic aspects of the geochemical approach to environmental problems as clearly and briefly as possible, it is convenient to refer to three levels of thinking at which the geochemistry of the environment is considered. These are the "grand strategic level", which includes broad generalizations upon which geochemistry is based; the "strategic level", which in this case involves the concepts associated with landscape geochemistry; and the "tactical level", which is concerned with the description of examples of the application of the landscape geochemistry approach to the solution of specific environmental problems.

WHAT IS GEOCHEMISTRY?

Geochemistry is the scientific discipline which is concerned with the role each element in the Periodic Table plays in the synthesis and decomposition of natural materials of all kinds. The "Grand Strategy" of Geochemistry is epitomized by the concept of the Geochemical Cycle (Figure 1) which is seen to be in two parts - a Major Cycle, which is essentially geological, and occurs within the Earth's crust; and a Minor Cycle, which occurs where the Lithosphere, Hydrosphere, Atmosphere, and Biosphere interact forming the weathering crust of the Earth. In this paper we are only concerned with the Minor Geochemical Cycle. It should be noted that, for a given element, the Liberation, Transport and Incorporation stages of the Minor Geochemical Cycle may not be completed in practice because at some stage the cycle may be halted indefinitely, short circuited or even have its direction reversed. But in spite of these limitations the concept of the Geochemical Cycle, when it is combined with the notion of the natural abundance of chemical elements, provides a useful overview of geochemistry which may be used as a starting point for a discussion of landscape geochemistry. Further information on general geochemistry may be obtained from the books by Clarke (1924), Rankama and Sahama (1950), Goldschmidt (1954), Mason (1966), Wedepohl (1970), and Fairbridge (1972).

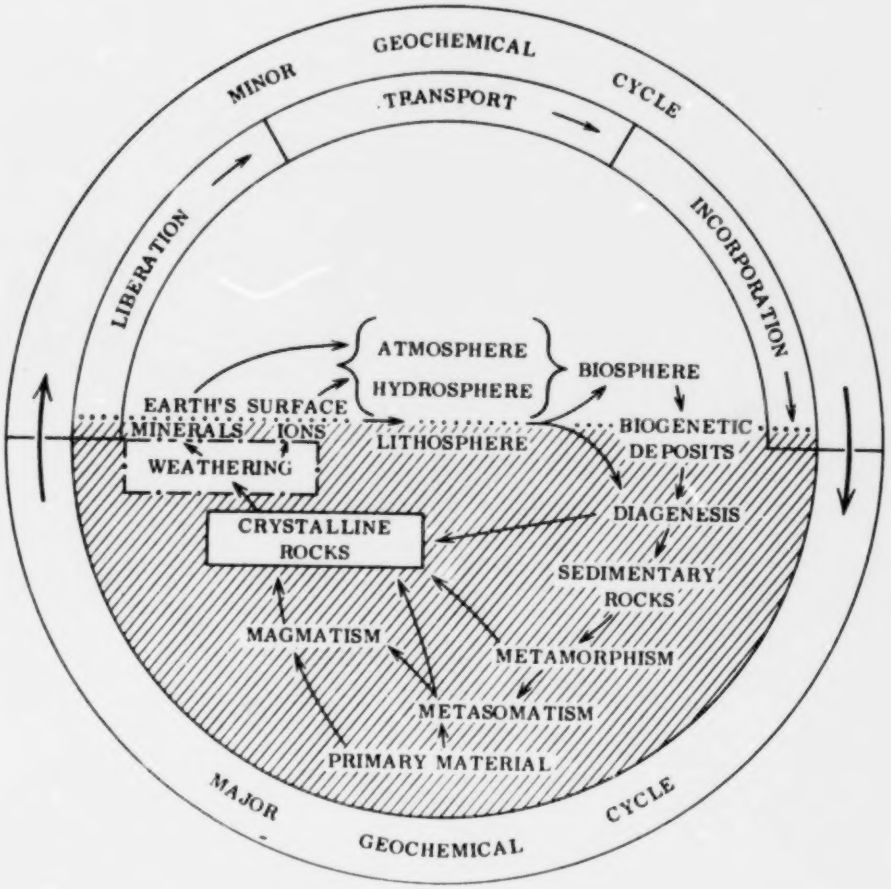
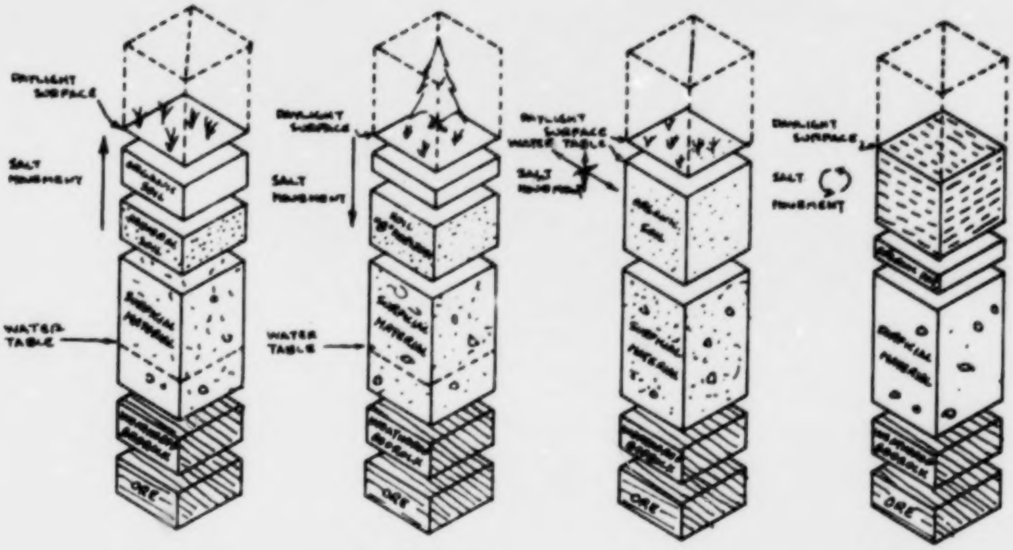

GEOCHEMICAL
MINOR
CYCLE
TRANSPORT
LIBERATION
INCORPORATION
ATMOSPHERE
HYDROSPHERE
BIOSPHERE
EARTH'S SURFACE
MINERALS
IONS
LITHOSPHERE
BIOGENETIC DEPOSITS
WEATHERING
CRYSTALLINE ROCKS
DIAGENESIS
SEDIMENTARY ROCKS
MAGMATISM
METAMORPHISM
METASOMATISM
PRIMARY MATERIAL
MAJOR
GEOCHEMICAL
CYCLE

FIGURE 1. THE GEOCHEMICAL CYCLE

[Modified from Mason (1958)]

WHAT IS LANDSCAPE GEOCHEMISTRY?

A simple definition of landscape geochemistry is "the study of the role chemical elements play in the synthesis and decomposition of natural materials which occurs at, or near, the daylight surface of the Earth under a given set of climatic constraints during geological time". Landscapes are said to be made up of a number of component parts (eg. rocks, soils, plants, animals, etc.) which chemically interact with each other resulting in the circulation of chemical elements through them. Strictly speaking, all landscapes may be related to four generalized conceptual models which were described many years ago by the Pioneer Russian geochemist B. B. Polynov (Glazovskaya 1963) as the "Elementary Landscape Types". Because of the complexity of landscapes it is often advisable to refer to them by block diagrams instead of describing them in words. On Figure 2 the four elementary landscape types are illustrated in this way by means of "prisms" extending from the unweathered bedrock to the atmosphere. Briefly, terrestrial landscapes are of two types: eluvial


DAYLIGHT SURFACE
SALT MOVEMENT
WATER TABLE
ORE
DAYLIGHT SURFACE
SALT MOVEMENT
WATER TABLE
ORE
DAYLIGHT SURFACE
WATER TABLE
SALT MOVEMENT
ORE
DAYLIGHT SURFACE
SALT MOVEMENT
ORE

Saline Soil
ILUVIAL
LANDSCAPE

Podzol Soil
ELUVIAL
LANDSCAPE

Organic Soil
SUPER-AQUAL
LANDSCAPE

Lake
AQUAL
LANDSCAPE

FIGURE 2. FOUR ELEMENTARY LANDSCAPE TYPES

[From Fortescue and Bradshaw (1973)]

landscapes where the annual precipitation exceeds the evaporation and illuvial landscapes where the reverse is the case. In cases where the daylight surface and the water table are coincident (i.e., in a marsh or bog), a "super aqual landscape" is found, and in a lake where the surface of the lithosphere is covered by a layer of water, a "subaqual" landscape is found.

One may well ask "What has all this to do with early-warning systems for toxic materials?" The answer to this question lies in the information obtained from tactical-level examples of landscape geochemistry carried out in the real world. But before these are described it is necessary to indicate briefly the present state of the art of landscape geochemistry. In Figure 3, a flow diagram is given

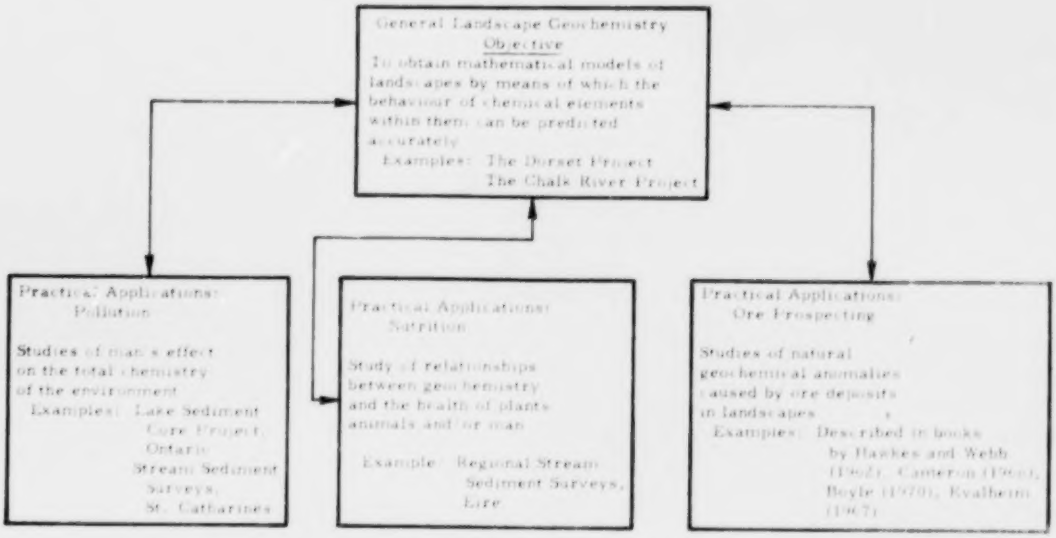
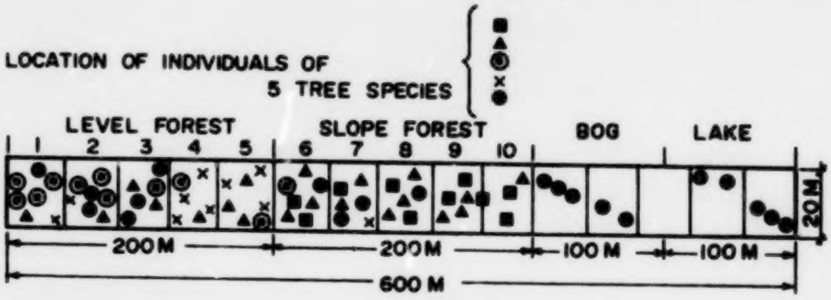
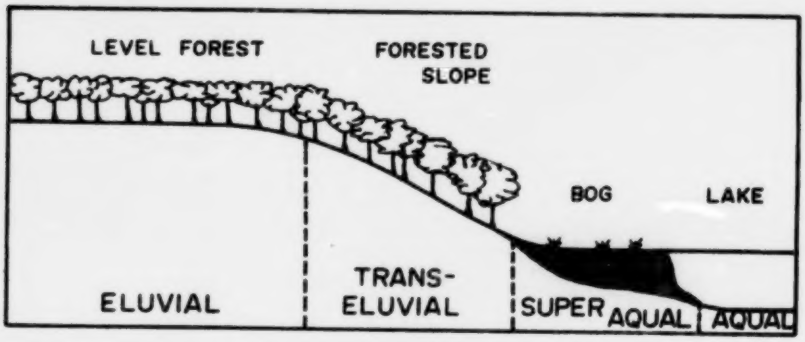

General Landscape Geochemistry
Objective
To obtain mathematical models of landscapes by means of which the behaviour of chemical elements within them can be predicted accurately
Examples: The Dorset Project
The Chalk River Project
Practical Applications: Pollution
Studies of man's effect on the total chemistry of the environment
Examples: Lake Sediment Core Project, Ontario
Stream Sediment Surveys, St. Catharines
Practical Applications: Nutrition
Study of relationships between geochemistry and the health of plants animals and/or man
Example: Regional Stream Sediment Surveys, Eire
Practical Applications: Ore Prospecting
Studies of natural geochemical anomalies caused by ore deposits in landscapes
Examples: Described in books by Hawkes and Webb (1962), Cameron (1961), Boyle (1970), Kvalheim (1967)

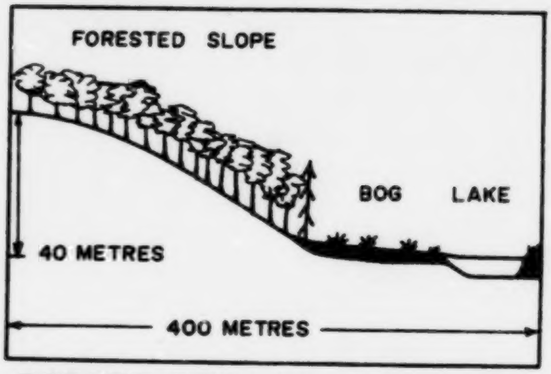
FIGURE 3. THE SCOPE OF LANDSCAPE GEOCHEMISTRY


LOCATION OF INDIVIDUALS OF
5 TREE SPECIES
■ ▲ ◎ × ●
LEVEL FOREST
SLOPE FOREST
BOG
LAKE
1
2
3
4
5
6
7
8
9
10
20 M
200 M
200 M
100 M
100 M
600 M

PLAN VIEW


LEVEL FOREST
FORESTED SLOPE
BOG
LAKE
ELUVIAL
TRANS-ELUVIAL
SUPER AQUAL
AQUAL

GENERALISED LANDSCAPE SECTION : CONCEPTUAL MODEL


FORESTED SLOPE
BOG
LAKE
40 METRES
400 METRES

DORSET PROJECT (diagram)

FIGURE 4. CONCEPTUAL MODEL OF A FORESTED LANDSCAPE SECTION AND A SCALE DRAWING OF THE DORSET SECTION [From Fortescue, et al. (1973)]

which indicates the potential scope of landscape geochemistry which involves practical as well as theoretical research. This flow diagram was included in order to focus attention upon the need to consider early-warning systems for toxic materials in relation to both the strategy and the tactics of the scientific discipline. The study of trace substances in the environment has, up to now, frequently lacked an intellectual superstructure at the strategic level of thinking. Consequently, much research time and money has been spent on projects which are essentially "isolated incidents" which cannot be directly related to any discipline. Let us hope that close attention will be paid to this point when scientists design early-warning systems for toxic materials. One way to promote such thinking is to offer a set of guidelines for the design of experiments which will be subject to review after a given period of time long enough for practical results to be obtained.

Examples of "Tactical Level" Investigations in Landscape Geochemistry

Example 1. A preliminary study of a forested landscape section at Dorset, Ontario

In June and July, 1972, a preliminary experiment was carried out at a specially selected landscape site on a forested hillside site located near Dorset, Ontario [Fortescue, et al. (1973)]. Very briefly, the site was selected for study on the basis of the conceptual model of a forested hillside shown in Figure 4 and includes a "transeluvial landscape" on a hillside adjacent to a "super-aqual landscape" located in a bog. Distribution patterns for a macronutrient (magnesium) four micronutrients (manganese, iron, copper, zinc), and two nonnutrient elements (aluminium and lead) were obtained from samples of -80 mesh soil material and tree branches taken at intervals of some 20M along the 400M section. We are concerned here only with the distribution patterns obtained for Aluminium and Lead (Figures 5 and 6).

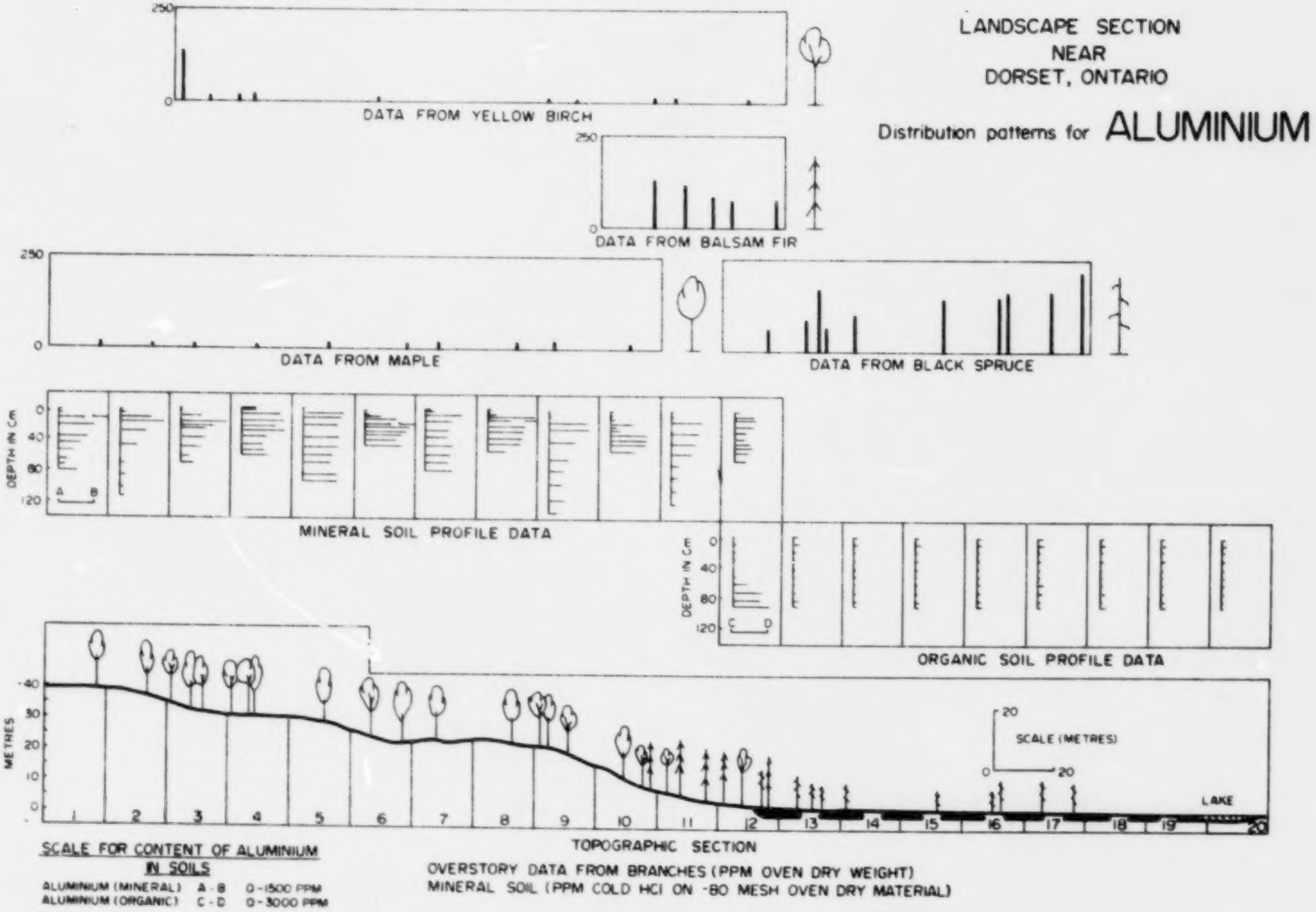


FIGURE 5. LANDSCAPE SECTION NEAR DORSET, ONTARIO - DISTRIBUTION PATTERNS FOR ALUMINIUM

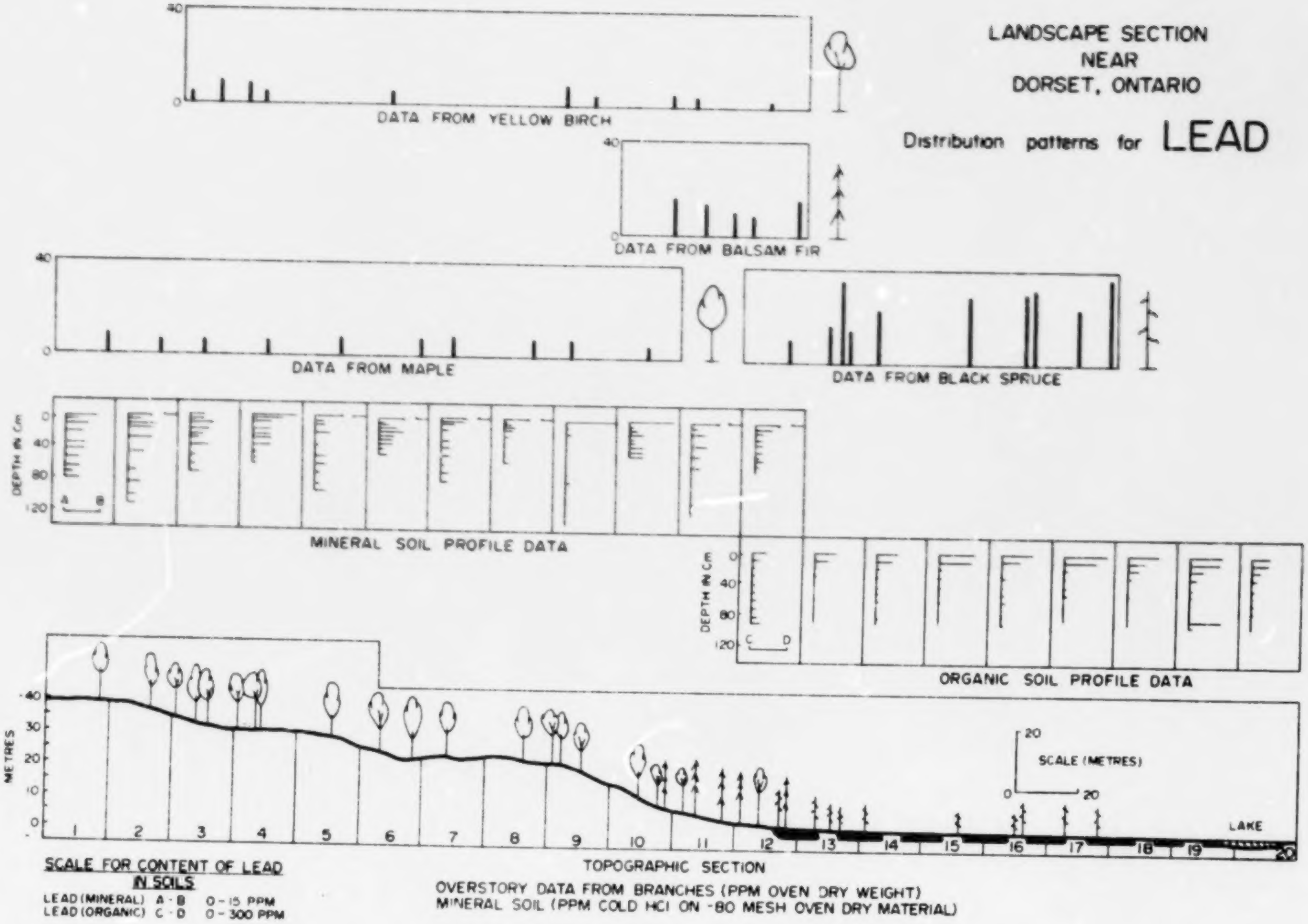


FIGURE 6. LANDSCAPE SECTION NEAR DORSET, ONTARIO - DISTRIBUTION PATTERNS FOR LEAD

Several points of interest regarding the natural distribution of these two elements in the plants and soils at Dorset are evident from the diagrams. The vertical distribution of aluminium is quite different in the mineral soil compared with the organic soil and there is no surface enrichment of the element in either of the soil types. The content of aluminium in the deciduous tree branches is consistently less compared with that in the coniferous species, and, in the Black Spruce there appears to be an increase in the content of the element in trees growing away from the bog margin.

The distribution of lead in the soils differs from that for aluminum because lead is accumulated - by the so-called "Goldschmidt Enrichment" - in the organic layers of the mineral soil and at the surface of the bog. More lead was found in the branches of the coniferous trees compared with the deciduous species and the amount of lead also tended to increase towards the center of the bog in the Black Spruce trees.

We can conclude from this preliminary experiment that chemical elements behave differently within the same landscape type as distribution patterns vary from element to element according to their amount, distribution and chemical behaviour within the soil. It was also evident that different tree species growing on the same soil take up different amounts of chemical elements - using an oven dry weight of branch material as a basis for comparison. [(For further details see Fortescue, et al. (1973).]

Tactical-level experiments of this type may conveniently be related to strategic-level and grand-strategic-level thinking. From the strategic-level viewpoint the Dorset project is interpreted to indicate that characteristic distribution patterns for particular elements can be easily described in soils and plants taken from different landscape types which lie adjacent to one another. Variations in distribution patterns at one, or more, of a series of sites studied in this manner might be a valuable early warning system relating to modifications of the environment by chemical substances - for example added to the landscape in rain. From the viewpoint of grand strategy, studies of the type carried out at Dorset could be expanded to include not seven but all elements in the Periodic Table and not just in Ontario forests but all suitable types of forest. It seems clear that one contribution this type of study could make would be to provide base line information on the distribution of all elements (not just nutrients) in forests which could be used to detect modifications of the chemistry of the environment at an early stage in areas where this was suspected.

Example II. A preliminary investigation of a forest stand at Chalk River, Ontario

The trees growing at Dorset had grown normally for a period of at least ten years prior to sampling. But what happens to trees when their growth rate is reduced, or increased, by environmental changes? A preliminary experiment along these lines was carried out in an Aspen (*Populus tremuloides* and *P. grandidentata*) stand located at Chalk River, Ontario [Fortescue (1973a)]. Briefly, subsamples of branch material representing lead shoot elongation for each year of a ten-year period (from 1960 to 1969) were obtained from twelve individuals of each of three species (*P. tremuloides*, *P. grandidentata*, and *Betula papyrifera*). Each tree was close to being 50 years old. The object of the experiment was to discover the effect on the uptake of the micronutrient elements copper and zinc and the trace elements lead and nickel of changes in the growth rate of the popular trees brought about by an attack by the forest tent caterpillar (*Malacosoma disstria Hon.*) during the growing seasons of 1962, 1963, 1964, and 1965. The birch trees were not affected and used as controls.

The information obtained from this experiment is summarized in Figure 7 where the dotted lines at the bottom of the graphs indicate

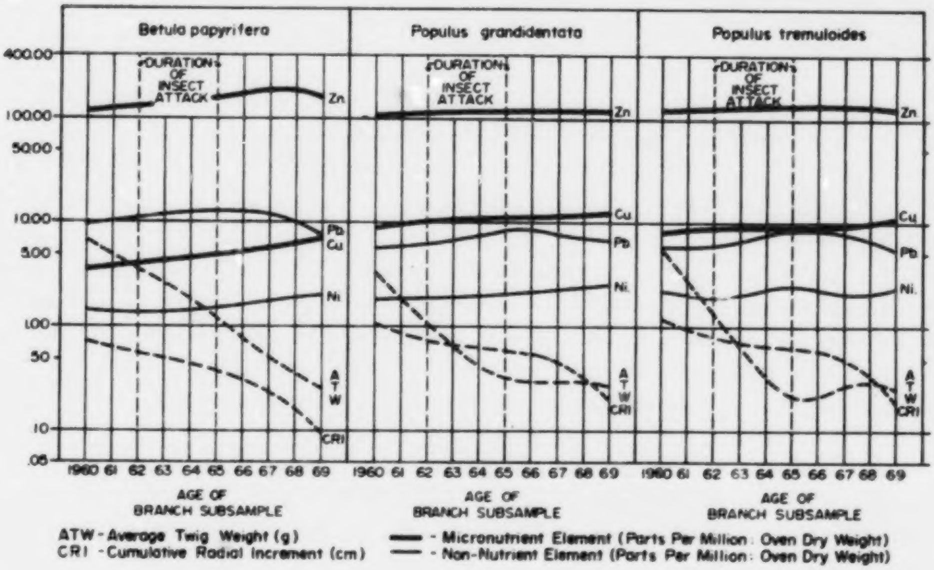


FIGURE 7. ESTIMATES FOR THE ELEMENT STATUS OF *POPULUS TREMULOIDES*, *POPULUS GRANDIDENTATA* AND *BETULA PAPYRIFERA* FROM THE PERCH LAKE ASPEN STAND, CHALK RIVER, ONTARIO, CANADA [From Fortescue (1973a)]

the growth rate of tree boles (cumulative radial increment) and branches (average branch subsample weight). The full lines indicate the concentration of each of the four elements in the branches over the 10-year period. The individuals of P. tremuloides were most affected by the insect attack which resulted in a minimum in the branch growth curve, associated with a maximum in the curves for the nonnutrient elements nickel and lead; whereas the curves for the micronutrient elements copper and zinc were unaffected.

This preliminary study indicates that nonessential trace elements in tree branches may be more sensitive indicators of changes in the chemistry of the environment than micronutrient elements and that experiments of the type described may be used as "history books" to describe the effect of toxic materials on trees. Studies along these lines might lead to the selection of tree species and chemical elements which were particularly sensitive to minute changes in the chemistry of the environment which could be used as a principle upon which to base an early-warning system.

This principle has been followed up on some detail by scientists interested in the effects of gaseous elements on plant growth. It has been known for some time that epiphites and lichens are particularly sensitive indicators of small amounts of sulphur dioxide and fluoride in the atmosphere. Further information on this interesting approach to the detection of changes in the environment may be obtained from the recent book edited by Ferry, Baddeley and Hawksworth (1973).

Example III. The use of lake sediment cores to detect man's effect on the chemistry of the environment

It was noted that at Dorset lead accumulated in the humus layer of the mineral soil and at the surface of the organic soil. Further information on the behaviour of this element in relation to man's activities was obtained from the study of lake sediment cores from Southern Ontario [Terasmae et al. (1973)], see Figure 8.

When European man came to Southern Ontario over a hundred years ago he logged the area and cleared it for agriculture. This disturbance is recorded by an increase in ragweed (Ambrosia sp.) pollen in lake sediments laid down at that time. Under favorable conditions a palynologist making an examination of a sediment core taken from one of these lakes (e.g., Puslinch Lake Figure 9) can date the part of the core laid down when the forested landscape was disturbed.

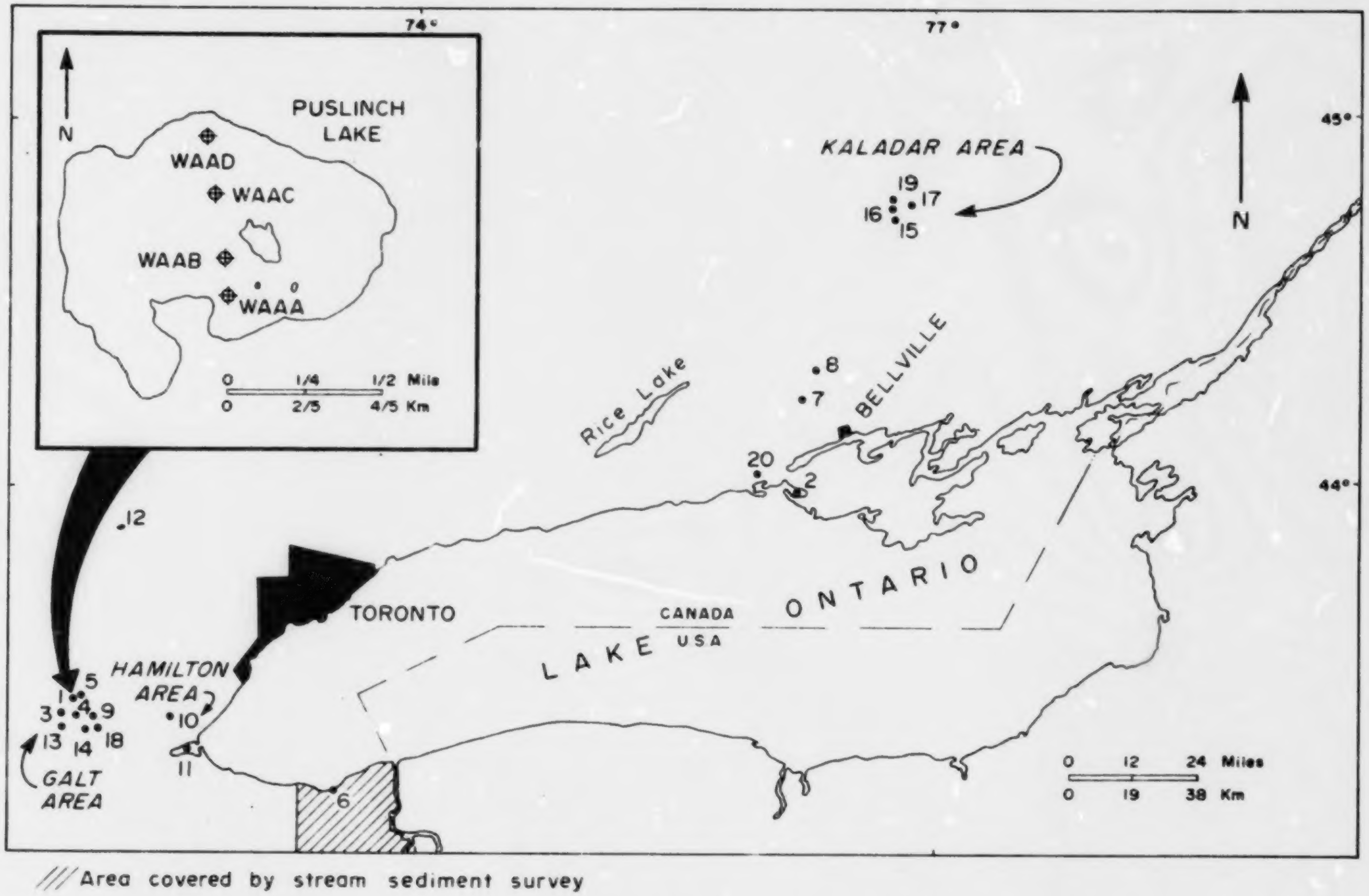

74°
77°
45°
44°
N
PUSLINCH LAKE
WAAD
WAAC
WAAB
WAAA
0 1/4 1/2 Mile
0 2/5 4/5 Km
KALADAR AREA
19
17
16
15
N
8
7
BELLVILLE
Rice Lake
20
2
12
TORONTO
CANADA
USA
LAKE ONTARIO
HAMILTON AREA
5
1
4
3
9
13
14
18
10
11
6
GALT AREA
0 12 24 Miles
0 19 38 Km
/// Area covered by stream sediment survey

FIGURE 8. INDEX MAPS SHOWING LOCATION OF LAKES SAMPLED AND AREA COVERED BY STREAM SEDIMENT SURVEY IN SOUTHERN ONTARIO AND LOCATION OF LAKE SEDIMENT CORE SITES IN PUSLINCH LAKE

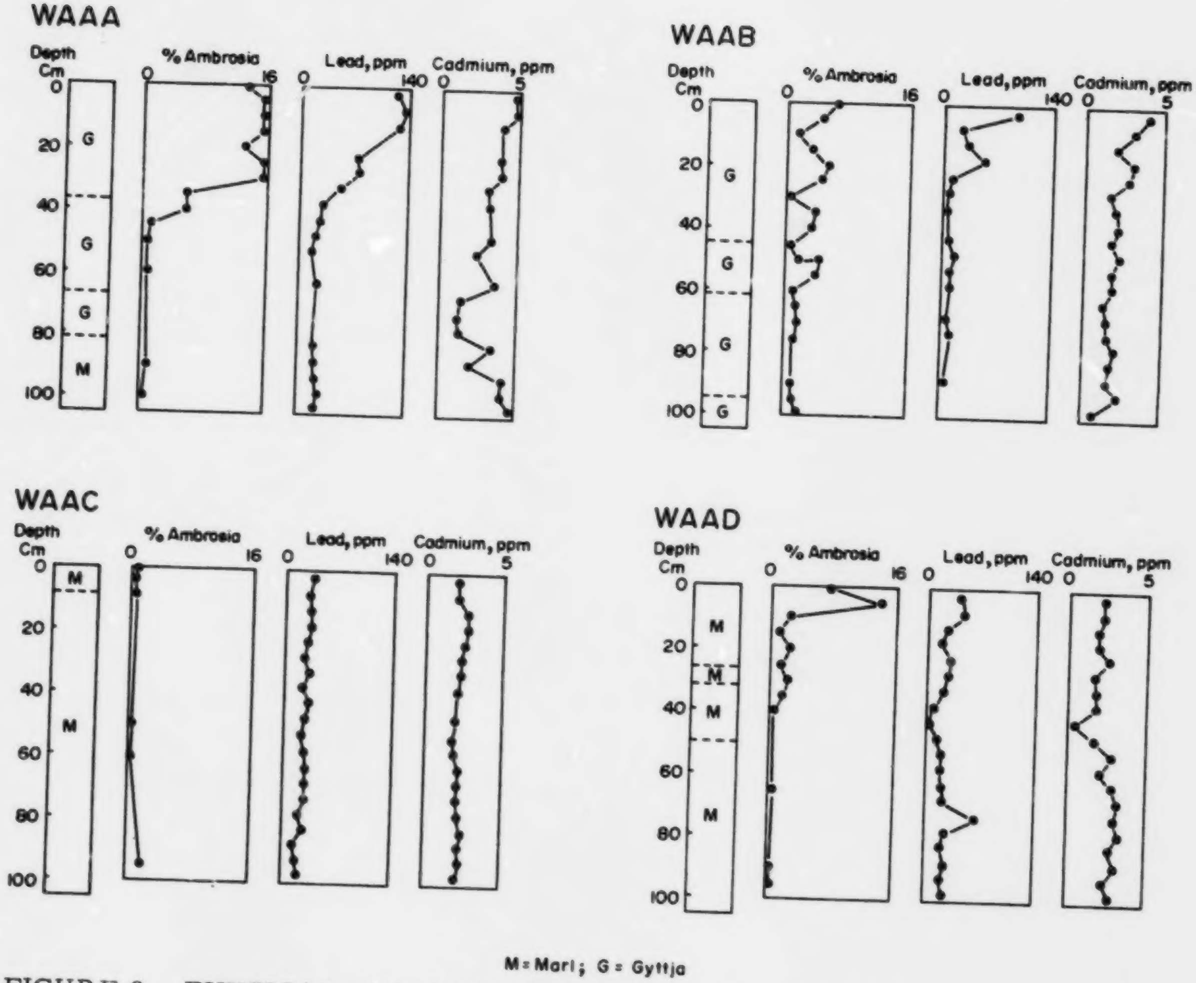


FIGURE 9. PHYSICAL, PALYNOLOGICAL AND CHEMICAL DATA ON FOUR LAKE SEDIMENT CORES FROM PUSLINCH LAKE, ONTARIO

[Terasmae et al. (1973)]

When the ash percentage, the copper content and the lead content in subsamples of cores is compared with the distribution pattern for Ambrosia sp. pollen in the cores it is seen (Figure 9 WAAA core) that lead increased in the core at the same time. We believe (Fortescue 1973b) that the increase in lead is associated with the breakdown of the forest humus brought about by man's activities in the drainage basins, although this relationship has not been worked out in detail.

From the viewpoint of early-warning systems for toxic substances, these patterns should be considered carefully because it may very well be that lake sediments hold a clear record of changes in the chemistry of a terrestial environment which can be explored in no other way. More generally, this is an example of how changes in the chemistry of one landscape type (e. g. , eluvial) may be detected in another adjacent to it (e. g. , subaqual).

Example IV. The use of stream sediments to detect natural — and man made — variations in the chemistry of drainage basins

During the past 20 years geochemical prospectors have repeatedly demonstrated [Hawkes and Webb (1962), Kvalheim (1967), Boyle (1971), etc.] that mineral deposits located in drainage basins can be located on the basis of data obtained from the chemical analysis of samples of dried, sieved, stream sediment material. More recently, the stream sediment approach has been used (Webb 1969) to detect imbalances in stream sediments associated with problems in agriculture. As a result of these activities, and others like them, it was decided in 1970 to make a stream sediment survey (suing the approach pioneered by geochemical prospectors) of an area of 450 square miles around the city of St. Catharines, Ontario in order to discover if the information obtained from it could be interpreted in relation to man's effect on the environment or variations in the geology of the area.

In Figure 10 the distribution of nickel in stream sediments collected from the St. Catharines area is shown at three levels of concentration (Class A: over 40 ppm, Class D: 11-20 ppm, Class E: 0-10 ppm). The Class A results were found to be in two clusters, one associated with an industrial plant in a rural area, and the other near industrial plants in Thorold, immediately south of urban St. Catharines. The dots and circles (1105 of them) on the Class D map (Figure 10) indicate the sample sites from which the stream sediment samples were taken. The dots indicate the relatively uniform distribution pattern of the most frequent concentration values. The Class E nickel values are seen to be concentrated along the shore of Lake Ontario and in the center of the south of the map where a "kame" (glacial feature) is located.

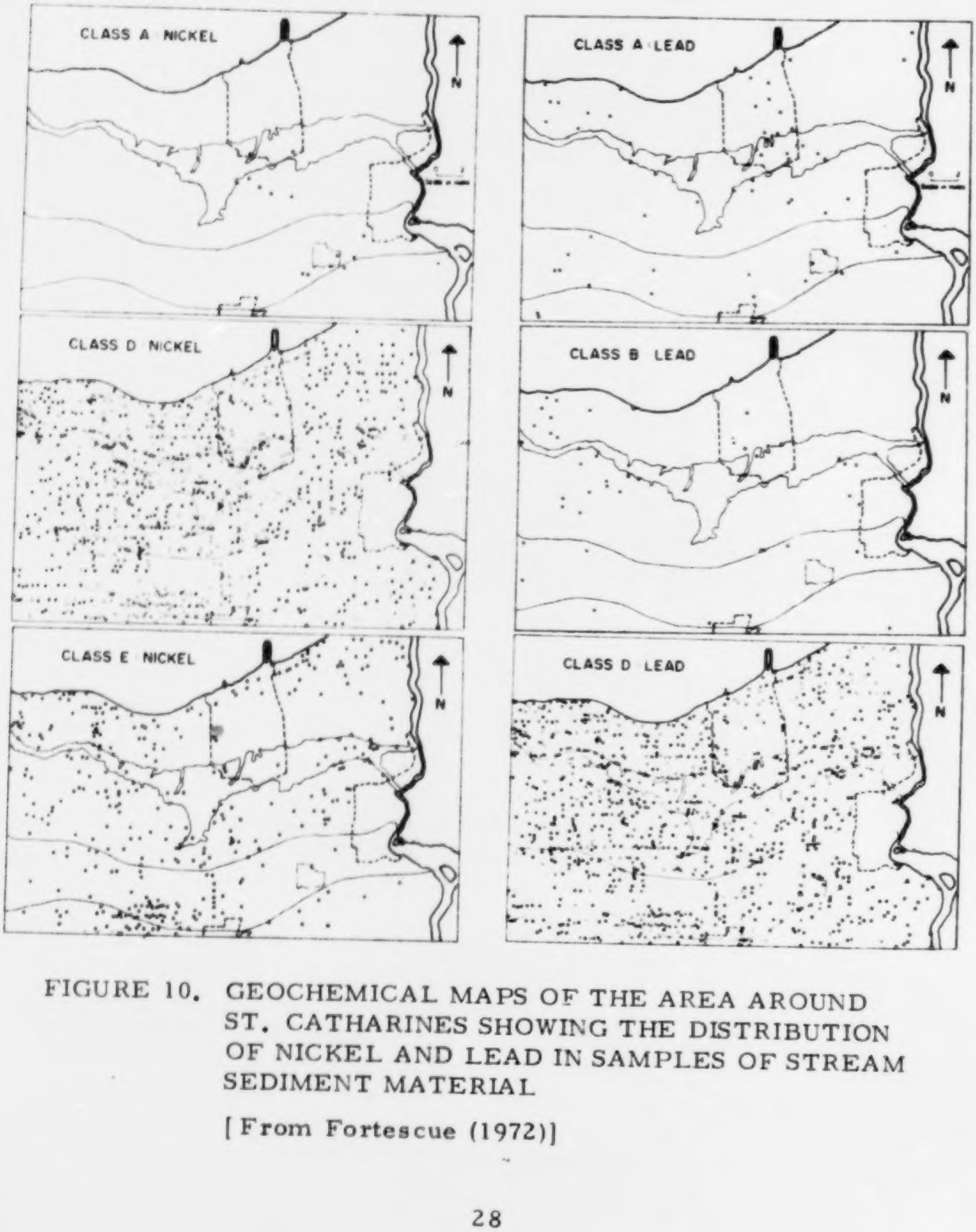

CLASS A NICKEL
N
CLASS A LEAD
N
CLASS D NICKEL
N
CLASS B LEAD
N
CLASS E NICKEL
N
CLASS D LEAD
N

FIGURE 10. GEOCHEMICAL MAPS OF THE AREA AROUND ST. CATHARINES SHOWING THE DISTRIBUTION OF NICKEL AND LEAD IN SAMPLES OF STREAM SEDIMENT MATERIAL

[From Fortescue (1972)]

The distribution of lead in the same stream sediment samples is shown in Figure 10. In this case the patterns are not so well developed as in the case of nickel. The Class A values (over 80 ppm) and the Class B (61-80 ppm) values are found in the St. Catharines - Thorold area and in the northwest of the area below the Niagara Escarpment where they are considered to be due to residues of lead arsenic sprays added to orchards. Other high values, to the south of the Niagara Escarpment (marked with an "R") are considered to be due to lead derived from the Lockport Dolomite, the bedrock underlying the area. [(Fortescue et al. (1971).]

In summary, the stream sediment geochemical survey approach may, under favorable conditions, be used to locate environmental variations in trace element patterns which relate to (1) Bedrock geology, (2) Pleistocene deposits, (3) Urban Industrial area, (4) Rural Industrial areas or (5) areas where trace elements have been added during fruit growing. It seems clear that the stream sediment survey approach should be seriously considered for early-warning surveys in areas where they may be suitable.

Example V. The use of stream sediments to locate an area characterized by molybdenum induced copper deficiency in cattle

A good example of the use of stream sediments to solve a problem involving the well-being of animals was described in a series of papers [Webb (1964), Webb and Atkinson (1965), Thornton et al. (1966)] published some years ago by geochemists from the Applied Geochemistry Research Centre at the Royal School of Mines in London who worked in an area in Co. Limerick, Eire. Briefly, stream sediment reconnaissance surveys revealed an area of some 30 square miles characterized by molybdenum and selenium anomalies related to an area of marine black shale. Detailed geochemical surveys, based on soils and pasture herbage, showed that high molybdenum occurred in these materials as well as in the stream sediments, Figure 11. An investigation of blood copper levels in cattle grazing in the area showed a highly significant correlation existed between areas of high molybdenum in the environment and areas where the cattle suffered from low blood copper.

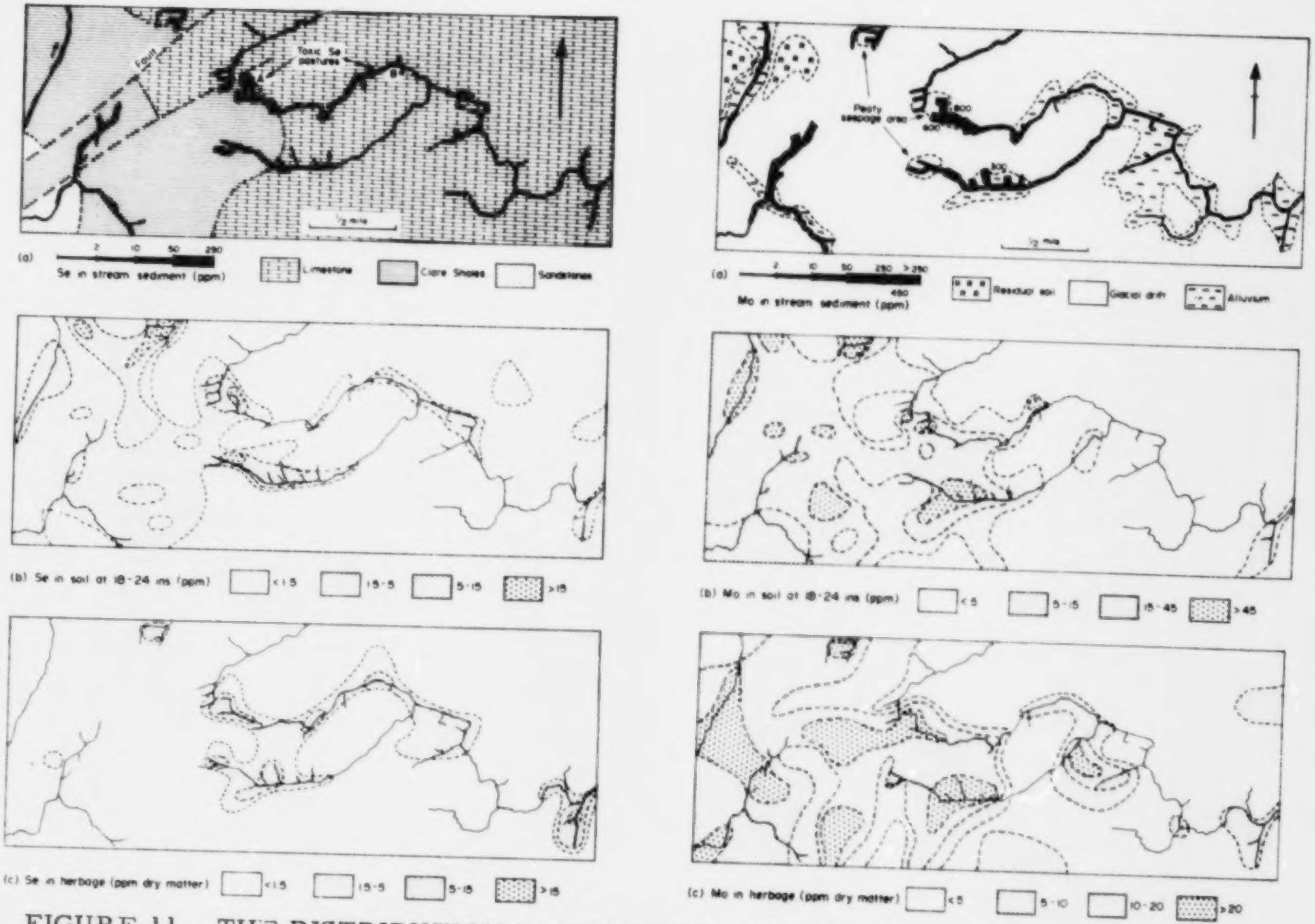

Fault
Toxic Se pastures
1/2 mile
(a)
2 10 50 290
Se in stream sediment (ppm)
Limestone
Clare Shales
Sandstones
(b) Se in soil at 18-24 ins (ppm)
<1·5
1·5-5
5-15
>15
(c) Se in herbage (ppm dry matter)
<1·5
1·5-5
5-15
>15
Peaty seepage area
800
600
300
1/2 mile
(a)
2 10 50 290 >290
480
Mo in stream sediment (ppm)
Residual soil
Glacial drift
Alluvium
(b) Mo in soil at 18-24 ins (ppm)
<5
5-15
15-45
>45
(c) Mo in herbage (ppm dry matter)
<5
5-10
10-20
>20

FIGURE 11. THE DISTRIBUTION OF SELENIUM AND MOLYBDENUM IN STREAM SEDIMENTS, SOIL AND MIXED HERBAGE COLLECTED FROM AN AREA IN CO. LIMERICK, IRELAND

[Redrawn from Webb and Atkinson (1965)]

Several points of interest to the design of early warnings for toxic substances may be pointed out in relation to this research. First, the study indicated that relationships between (a) bedrock geology, (b) stream sediment trace element content, (c) pasture soils, (d) pasture herbage and sickness in cattle could be established with the minimum of effort. Second, the study showed how the toxic effects in the cattle (i.e., low blood copper) resulted from an interaction between excess molybdenum and copper and was not related to the level of copper in the herbage. A third aspect of this study was that the amount of molybdenum in the herbage was not constant the year round but varied with season which further complicates investigations of relationships of this type. Clearly, a case can be made for the consideration of a Landscape Geochemical approach to the solution of similar complex problems in other areas once they are identified.

SUMMARY

In this paper we have reviewed briefly aspects of the Geochemical approach to the solution of environmental problems. To begin with it was noted that geochemistry can be studied at three levels of thinking called here "grand strategic", "strategic", and "tactical". In the second part of the paper five examples of environmental geochemical investigations were given in order to indicate how the Landscape Geochemical approach might be used to provide early warning of toxic materials in the environment. It should be stressed that much research along the lines described is needed before the reliability of geochemical methods for early warning of toxic materials in the environment can be considered established. Such research would be most effective if it were designed on the basis of "strategic level" rather than "tactical level" thinking so that sets of comparable information are collected while experience is being gained.

CONCLUSIONS

Scientists involved in the design of experiments in relation to early-warning systems for toxic materials research might consider the grand strategy, strategy, and the tactics of the landscape geochemistry approach to the solution of environmental problems with profit so that guidelines may be established which will result in the collection of information packets which can be carefully related and compared with each other.

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LEGISLATION AND LAWS CONCERNING EARLY WARNING SYSTEMS FOR TOXIC SUBSTANCES

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ABSTRACT

The existing statutory basis for the control of the manufacture, distribution, and disposal of toxic chemicals is reviewed. Included are pesticides, drugs, food additives, cosmetics, chemicals threatening occupational safety, and radioactive materials.

Unregulated hazards are described as well as pending legislation to deal with such hazards. Of primary importance are the environmental effects of a number of consumer products, including detergents and products containing heavy metals.

Finally, the relevant considerations Congress must weigh in establishing "early-warning systems" for toxic substances are described. Alternatives are discussed with particular emphasis on the "Toxic Substances Control Act of 1973" now pending in Congress.

INTRODUCTION AND DEFINITION OF TERMS

As my assignment this morning is to review existing statutes and pending legislation in the Congress dealing with early-warning systems for toxic substances, it might be fruitful at the outset to define the limits of my presentation and to describe some of my own limitations with respect to defining the means of controlling toxic substances.

My work on the staff of the Committee on Commerce deals primarily with assisting the Committee with science matters associated with environmental legislation. Although I haven't worked directly in the field for about 4 years, I nonetheless still regard myself as a fish and wildlife biologist. I profess to less and less identification with that occupation, however, as in recent years my function on the Committee staff has been less in the area of scientific interpretation and more in the area of legislative drafting and escorting legislation through the Congress.

In terms of describing my biases in helping formulate regulatory policy for the control of toxic substances, it should be noted here that I have a very high affinity to the Senate-passed version of the Toxic Substances Control Act, having been associated with it since Senator Magnuson introduced the first version some three years ago on behalf of the Administration. Thus, if I seem more a cheerleader for this pattern of regulating the chemical substances rather than an impartial observer, you now have the reasons why.

Obviously, the notion of "early-warning systems" can mean a great many things. Not only can it mean the extent to which regulatory authorities are given a look at safety data and an opportunity to control substances before they are put to their respective uses, but it can also encompass the entire range of monitoring the presence of chemicals in the environment, monitoring environmental indicators, the reporting of chemical use by manufacturers, and a number of other techniques. In order to appropriately limit this presentation, however, it is my intention to deal only with the means by which regulatory control is applied prior to the marketing of potentially toxic chemicals. To go beyond this limitation would strain not only my abilities but your patience as well.

In doing so, it would seem appropriate to give a brief description of the types of premarket review now applied to a variety of chemicals which could be termed "toxic chemicals" and to review as well proposals for change now pending in the Congress. Finally, I will discuss briefly some principles of premarket review which might serve to clarify public policy questions for the regulation of chemicals.

To further limit the scope of this paper and to keep the focus within an area for which I feel comfortable, I intend to deal only with the regulation of those chemicals which fall under the heading of pesticides, drugs, food additives, cosmetics, air and water pollutants, and the broad categorization of environmental pollutants which fall through the cracks of existing regulatory programs.

EXISTING PREMARKET REVIEW MECHANISMS

Pesticides

Along with drugs, the regulatory mechanism in existance for pesticides contains the most severe requirement for premarket scrutiny by a regulatory agency of all the toxic substances regulated by the Federal Government. As I am sure most everyone in this room is aware, the Environmental Protection Agency must grant registration to each new chemical to be used as a pesticide before it can enter the channels of commerce. In order to grant registration, EPA must be satisfied that unreasonable burdens to man or the environment will be avoided through the intended use or misuse of the prospective pesticide. As the burden of making this determination falls on the manufacturer, the data in support of the registration must be furnished by the manufacturer.

Drugs, Except Antibiotics and Insulin

A similar premarket review requirement exists for drugs. Under the Federal Food, Drug and Cosmetic Act, each manufacturer of a new drug must submit a "new drug application" which must be approved by the Food and Drug Administration before the drug can be marketed. Again, the manufacturer is responsible for furnishing the data necessary to make the determination that no undue adverse effects are associated with the drug.

Food Additives, Antibiotics and Insulin

Food additives, antibiotics, and insulin are all treated in much the same manner under the Federal Food, Drug and Cosmetic Act.

With respect to antibiotics and insulin, when a specific use is approved by FDA, a monograph is issued. Subsequent manufacturers of the specific antibiotic or insulin for the specific uses intended need not obtain further FDA approval prior to marketing.

Food additives are treated in much the same way. Once a petition for approval of a food additive has been approved by FDA, subsequent manufacturers of the same food additive for the same purpose need not get individual clearance from FDA for marketing. If he determines in his own mind that he is marketing the same food additive for the same food he is free to do so.

The primary distinction with this type of early warning system as opposed to that in effect for drugs and pesticides is that the manufacturer need only satisfy himself that he is in compliance with either a monograph or an approved petition rather than convincing either FDA or EPA of its compliance. Obviously, the burden of proving safety or a lack thereof falls on different shoulders in each case.

Cosmetics

There is no premarket review of the ingredients of cosmetics other than coloring.

With respect to cosmetics, FDA can only take action when it proves a hazard exists from an ingredient of a cosmetic. Again, the burden is on the Food and Drug Administration to prove the hazard rather than the manufacturer proving the lack of hazard. And in most cases this information will only become available after the cosmetic is on the market.

Air and Water Pollutants

Air and water pollutants present a special case as regulatory mechanism is directed not at product composition, but rather towards protection of specific environmental mediums through the application of municipal and industrial effluent and emission control.

Importantly, neither the Clean Air Act nor the Federal Water Pollution Control Act contains a mechanism for the premarket or premanufacture review of environmental health and safety data for chemical substances.

Environmental Contamination From Consumer Products

The most important class of environmental contaminants which is as yet unregulated are those constituents of consumer products which have slipped through the cracks of existing regulation for environmental effect. These are materials which are not pesticides, drugs, food additives, or cosmetics. Rather, we are talking about phosphates in detergents, heavy metals and other constituents of consumer products like paint and drain cleaner for example, PCB's, packaging, and a wealth of other potential hazards. Included are all the consumer products which either escape sewage treatment or proper solid waste disposal or are more efficiently controlled by regulating the product rather than its disposal. For example, rather than remove the phosphates from sewage effluent in the Great Lakes, it may be far more prudent to control phosphates in detergents at the production level.

It is these types of hazards that the proposed "Toxic Substances Control Act" now pending in Congress is designed to control.

LEGISLATION PENDING IN CONGRESS

Limiting the definition of an "early-warning system" as I did somewhat arbitrarily in the first part of this paper, the amount of proposed legislation to be examined is considerably lessened. Of course, any mechanism that assures that scientists and regulatory agencies obtain good scientific information at as early a time as possible will help to prevent problems before they become manifest. Obviously, a great deal of legislation is pending to provide that assurance. However, with respect to altering the system of regulation prior to marketing, there are two significant gaps that remain. The first is the environmental effects of consumer products mentioned previously. The second is the premarket review of safety data on cosmetics.

Cosmetics

Cosmetics obviously do not present the same type of hazard as a chemical with broad distribution or more intimate contact with biological systems. Neither are we talking about chemicals which would greatly disrupt our economic system if premarket review of some kind were afforded. As cosmetics have been known to present at least potential health risks, mercury in face creams, for example, some type of premarket review of safety data would seem justified.

Several bills have been introduced in the Congress which would provide for such premarket review.

In the Senate, a primary proponent, I am happy to say, has been Senator Magnuson along with Senator Eagleton. Senator Magnuson's bill would require that each manufacturer of a cosmetic now get the approval of the Food and Drug Administration before marketing. The bill also contains a means of obtaining safety data on existing cosmetics. Senator Eagleton's bill is similar as is legislation introduced in the House of Representatives by Congressman Paul Rogers. It is probably safe to say that the Congress will not act soon on any of these proposals. (2) To my knowledge, the relevant committees in either the House or the Senate have not yet held hearings on the legislation. Given this, it appears unlikely that early action will occur.

Toxic Substances Control Act

The Senate version of the Toxic Substances Control Act, introduced early last year by Senators Hart, Magnuson and Tunney could be described as a fourth generation descendant of the original Administration proposal. That the bill has been around this long is ample testimony to the complexity of the issues involved and to the controversies surrounding it.

The pre-market review procedure contained in the Senate-passed Toxic Substances Control Act differs substantially from the laws regulating pesticides, drugs, food additives, and cosmetics. The primary reason for the unique procedure is the tremendous number of new chemicals which are developed and which could conceivably be regulated by the Toxic Substances Control Act. The coverage is necessarily broad in order to insure that new chemicals found in consumer products and new uses of existing chemicals found in consumer products will be encompassed by the umbrella of regulation. Although it is difficult to predict the exact number of chemicals so encompassed, a report prepared by the Council on Environmental Quality estimates that several hundred per year would fall into this category. (1) The Committee on Commerce thought it extremely important to streamline as much as possible the premarket review mechanism in order not only to avoid administrative burden, but even more importantly, to lessen the burden of delay on the chemical industry that would exist if a standard premarket clearance procedure remained.

The House version, on the other hand, does not contain the notification provision. Under that bill, EPA would only get notice of those chemicals for which a prior determination of "substantial danger" has been made.

The mechanism chosen requires each manufacturer of a new chemical substance to give notice to the EPA 90 days in advance of the commercial production of any new chemical or new uses of existing chemicals. For those chemicals which EPA has predetermined to be of questionable safety, test data would have to be submitted along with the notification. During the premarket review period, EPA would have the authority to impose restrictions on the use or distribution of the substance or could extend the 90 day premarket screening period for an additional 90 days. The legislation is drafted in a manner which gives EPA broad authority to so limit the use or distribution of a chemical during this period.

The primary difference between the premarket screening mechanism envisioned by the Senate bill and existing premarket clearance procedures is that EPA must take affirmative action during the premarket screening period to stop a chemical's production. Under the pesticide and drug laws, EPA must take affirmative action to let a chemical on the market. The Senate language is designed to lessen the substantial fears of the chemical industry over EPA lethargy in granting approval. At the same time, given the broad discretionary authority that EPA would possess during the premarket screening period, there is ample authority to prevent unreasonable risks before the production, distribution and use of the chemical is irrevocable.

PRINCIPLES OF PUBLIC POLICY WITH RESPECT TO EARLY-WARNING SYSTEMS

On the basis of some familiarity with at least one of the proposed early-warning systems for the control of toxic substances, let me propose some principles that might be useful in developing public policy on early-warning systems. Obviously it is difficult to formulate specific principles from the track record of the Congress as Congress has not been entirely consistent, legislating thoroughly in some areas and leaving others virtually untouched. But at the risk of stating the obvious, let me mention briefly two principles which stand out in my mind.

First, the extent to which premarket review is given and the structure of that review must hinge on the likelihood of finding unbearable threats and an assessment of the magnitude of those threats. This must be balanced against the effect of delays on the affected industry. In other words, the extent to which inconveniences and delay are placed must depend on how frequently intolerable risks will be found and what the magnitude of those risks will be. In the case of chemicals which have the specific purpose of altering biological systems, like pesticides and drugs, the answer, at least to me, is very obvious. These chemicals should not be disbursed to man or entered into the environment until we are reasonably sure of the threat and have made a judgment that the threat is tolerable.

On the other hand, when we are looking for environmental threats from perhaps a few out of several hundred chemicals with little chance for a direct adverse effect on human health, we can stand to be less rigorous in our premarket review. As I perceive it, that is the principle which has been applied to the premarket screening provisions of the Senate-passed version of the Toxic Substances Control Act.

The second broad principle one could delineate is that the greater the latitude given an agency prior to market, the greater the assurance must be that indeed that discretion is executed properly. The means to provide that assurance are usually found in the extent to which scientific and technical information is released by the regulatory agency and the extent to which judicial review of agency decisions is provided. Both of these issues are very difficult to resolve as several valid competing considerations are often at work.

With respect to releasing information, obviously much of what is received by the regulator has competitive value. Data with respect to intended uses, chemical formulas, and industrial processes are highly valuable pieces of information and usually are protected from release. On the other hand, in the hands of impartial scientists, toxicological data, physical and chemical specifications, and other data can be scrutinized and input sent back to the regulators. On the other hand, government agencies are seldom anxious for this type of input. The principle used in formulating the Toxic Substances Control Act in the Senate has been to release as much of these data as can be released without causing significant competitive injury. This could allow the release of certain toxicological and other data for review by the scientific community. In the case of a chemical which is patented, and the owner is protected, a great deal of information would be released. If it is not, however, and release of this information would significantly hurt him competitively, the manufacturers data would be withheld.

The question of the extent to which the courts may review administrative decisions is a question of enormous significance. Historically, under the Administrative Procedure Act, administrative decisions may only be overturned if the court finds that the decision was reached arbitrarily or capriciously or is not supported by substantial evidence. While these terms have been defined by the courts in a number of ways, the prevailing principal is that it is extremely hard to overturn agency decisions in court on the merits of the case. Rather, most appeals of administrative decisions center around whether the procedural requirements of the decision-making process were violated. Rarely are the merits examined in any great depth.

I find this disheartening perhaps owing to my lack of legal training. Certainly, proper procedures must be followed, but I would think it entirely healthy for the administrative process if the courts were allowed to examine the merits of the Administrative decisions in greater detail. History remembers Christopher Columbus as the man who landed in San Salvadore in the Bahamas, not as the man who took several wrong turns in getting there.

Certainly in matters of technical judgment, the expertise of the administering agency should not be taken lightly. Nor should the lack of technical expertise on the part of judges. In cases where technical matters can be understood, however, and the judge satisfies himself they can be understood, it does seem entirely fitting that greater latitude should be given to the courts to decide cases on the merits.

As a footnote to this discussion, I should point out that there has been little movement toward this end in the Congress. In fact, far greater progress has taken place at the State level where a number of States have given the courts near-blanket authority to review administrative decisions on environmental matters.

Should the principle be developed on a broader scale, the quality of the administrative decision making should be vastly improved.

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AN INCIDENT OF INDUSTRIALLY RELATED TOXIC PERIPHERAL NEUROPATHY

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ABSTRACT

Results of an ongoing investigation of an outbreak of toxic peripheral neuropathy among workmen employed in a fabrics coating plant indicate that of 128 individuals given complete neurological examinations, 53 have been diagnosed as having a definite polyneuropathy. Although the etiological agent(s) has not yet been conclusively determined, an organic solvent(s) used in the printing operations is highly suspect as a possible cause of the problem. This case will be used as an example to point out the inadequacies in available toxicological information and to emphasize the need for systems of early warning.

INTRODUCTION

I will describe a recent outbreak of toxic peripheral neuropathy among employees in a fabrics coating plant as an example to point out the inadequacies of presently available toxicological information and to emphasize the need for a comprehensive early warning system capable of identifying, in advance, the potential for this type of problem.

CASE REPORT

In mid-August 1973, the Ohio Department of Public Health was apprised by the Neurosurgery Service of the Ohio State University Hospital of a case of peripheral neuropathy suspected to be of toxic origin. The patient, a 43 year old male employee of a plant producing vinyl-coated wall coverings, complained of having been weak since May. Medical examination revealed that the onset of the disorder had been quite insidious. The initial signs included a gradual development of tiredness or weakness of muscles, extending over a period of months. Sensory findings became evident as intermittent paresthesias in the hands and feet as if the fingers were asleep. Some aching sensations in the arms and legs were also present. Although there was unexplained weight loss, it is of interest that there were no symptoms of gasterointestinal disturbances, cutaneous lesions, loss of hair, autonomic symptoms or disturbance of vision. Electromyography confirmed the diagnosis of a relatively acute peripheral neuropathy.

The patient also revealed that five or six other employees in his department of the plant (the print department) had similar symptoms.

An investigation was immediately initiated by officials of the Division of Occupational Health, Ohio Department of Public Health. Their evaluation confirmed that, indeed, there were six other employees in the print department of the plant who were diagnosed with peripheral neuropathy and that the problem perhaps involved many other employees in several associated departments in the plant. The investigation further revealed that chemicals such as hexane, acrylamide, tri-o-cresyl-phosphate, or thallium, commonly known to produce a toxic neuropathy, had not been in use in the plant for more than 10 years. The only significant change in operation or process was a substitution of normal methylbutyl ketone (MBK) for methyl-isobutyl ketone (MIBK). The ventilation system, particularly in the print shop areas of the plant, was noted to be grossly inadequate, principally due to poor design and maintenance. Poor work practices were a significant contribution to exposure – including eating at the work site and using solvents as a skin cleaner. Because of the serious nature of the problem, the uncertainty of the cause, and the potential nationwide implications, one of the most intensive and concerted occupational health investigations in this decade was initiated involving several state, federal and private organizations.

Medical examinations including electromyograms (EMG) were performed on 1,156 employees – practically the entire workforce of the plant. Those with abnormal EMG findings were given a thorough neurological evaluation. In order to better characterize the disease and to quantify the degree of involvement, Dr. Norman Allen, Ohio State University, and his colleagues developed a rating scale in which numerical values were assigned to:

a. Symptoms illicited from medical history

b. Neurological examination findings

c. Electrode diagnostic studies.

Any total score of 9 or above was classified as a definite polyneuropathy. Of the 128 individuals rated under this scheme, approximately 50 were found to have symptoms, signs and EMG's consistent with a definite, acute, peripheral neuropathy not attributable to other known causes.

Epidemiologic investigations revealed that the majority of affected employees worked in the print department where a mixture of MEK and MBK was used in large quantities as a solvent. It was shown that, with one or two exceptions, all definite cases of neuropathy had exposure to essentially the same chemical substances as did those working in the printing areas. Printing machine operators, who had the highest attack rate as a group, were exposed to the highest concentrations of solvent vapors. In addition, they had significant exposure through other routes. Work practices and a lack of protective clothing offered potentially excessive skin exposure. Employees eating on the job demonstrated a greater risk of acquiring the disease than those who did not. Finally, the affected employees worked significantly more overtime than non-affected employees. Neither MBK nor any of the other agents used in the plant have previously been associated, as far as we know, with this particular type of illness.

The facts or circumstances which implicate MBK as the possible etiological agent are as follows:

1. MBK was first used in the plant in August, 1972, and was put into full use by December, 1973. The first symptoms of the disease appeared in December, 1973.

2. No other changes in the materials or processes were identified.

3. Workers in an almost identical coated fabrics operation on the west coast had similar exposures except that MBK had never been used in that plant. Although they were examined in a similar manner, none of these workers were found to have any evidence of peripheral neuropathy.

4. Two isolated cases of peripheral neuropathy in Connecticut and Iowa with signs and symptoms very similar to that described here also were occupationally exposed to MBK.

5. Chemicals commonly known to cause peripheral nerve damage have essentially been ruled out on the basis that they have not been used and no evidence of their presence has been detected by laboratory analytical evaluation of materials used and biological samples obtained from affected workers.

I am sure that there are many isolated cases of peripheral neuropathy for which no cause is ever discovered, even after extensive investigation. When this happens, any chemical in the patient's environment can be a scapegoat. Some of the reports of alleged chemical neuropathy are not very convincing and once a substance has been blamed for a particular toxic effect, the case against it may be self-perpetuating. I fear that this kind of situation may hold here and in spite of the fact that we have stated that a causative has not yet been conclusively established in this case, I note from articles in the press and based on some industries withdrawing it from use in their plants that MBK has been tagged as a peripheral neurotoxin.

The results of animal studies presently underway will be critical in determining the actual cause of the problem.

The use of a large number of chemical compounds in this plant, many for which there is little or no toxicological information available, has markedly complicated the assessment of the problem. In our investigation, one of the first steps was to obtain a comprehensive list of all chemical raw materials used in each area of the plant. You might be surprised at what a difficult task this is for some companies. In this case, for some of the compounds, the company was able to provide only the supplier's tradenames. For some, the company had no idea what actual chemicals by scientific name they were using - much less, information about the toxicity. This points out the need for some uniform system whereby the purchaser of a chemical substance is able to identify the compound that he is using and to have information on its toxic effects, special precautions, symptoms of exposure, etc. Section 20(a)(6) of the Occupational Safety and Health Act of 1970(1) requires the Secretary of the Department of Health, Education, and Welfare to publish, on an annual basis, a list of all known toxic substances and the concentration at which such toxicity is known to occur. The 1973 list(2) contains over 12,000 compounds for which published toxicity information is available. The Occupational Safety and Health

Administration (OSHA) has promulgated safe exposure standards for only 450 chemical substances.(3)

That gives you an idea of where we are in terms of just basic toxicological information. The research required to develop sufficient data to establish safe industrial exposure standards for all the potentially toxic chemical compounds in use is astronomical. Additionally, while gross manifestations like coma or convulsions are readily recorded and attributed to actions of a poison on the central nervous system, effects on the peripheral nervous system may escape notice. Detailed studies of functional and structural changes in the central and peripheral nervous systems do not often get carried out in conventional toxicity tests.(4)

These kinds of studies address a single agent concept while it is a rare situation indeed when a workman in an industrial situation is exposed to only one toxic chemical compound. More typically, workmen are subjected to a variety of chemical agents as well as to noise, heat, radiations, and vibrations - all superimposed on the additional stresses resulting from various psychological or motivational factors associated with the workplace.

Although the synergistic, additive, potentiation and antagonistic actions of some combinations of environmental contaminants have been documented, there has been relatively little work done in this very important area. When one thinks of all the possible combinations and permutations of the thousands of chemical and other stresses that would require study, it is practically impossible to know where to begin. Recognizing that present collective resources available to attack this type of problem can only scratch the surface of the issue, it is imperative that an effective and responsive system be developed whereby research priorities can be established that are appropriate to the needs of a variety of organizations and agencies concerned with toxic substances.

In closing, I would like to add a word of caution in the context of the theme of this seminar. A system of early warning for toxic substances certainly depends on the availability of appropriate toxicological information - but that in itself is not enough. Some mechanism is required whereby the potential for exposure can be identified and a means of assuring that exposures are effectively controlled so that an incident like I have just described is prevented. The "system" might well tell us that compound A in combination with compound B at x concentration for y days will cause peripheral neuropathy and even that these types of exposures are likely to occur in a particular type of industry, but if we do not have a mechanism to impart that information to the appropriate people who must take action to see that it does not occur, then we will continue to see these types of episodes.

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ESTABLISHING ENVIRONMENTAL PRIORITIES FOR SYNTHETIC ORGANIC CHEMICALS: FOCUSING ON THE NEXT PCB'S

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ABSTRACT

Well over 9000 synthetic organic chemicals are produced in commercial quantities and annually total approximately 140 billion pounds in the United States. Many of these chemicals, such as pesticides, detergents, PCB's and phthalic acid esters, have become well recognized environmental contaminants. Because of the large number and quantity of organic chemicals being produced, a procedure to set priorities for environmental research, monitoring, protocol testing (e.g., persistence and toxicity), and regulatory action is necessary.

This paper discusses (1) the parameters which are important to establishing such a procedure, (2) the quantity and quality of the information presently available as well as potentially available after the passage of the Toxic Substances Control Act, and (3) the difficulties of integrating the parameters to provide an overall ranking of the chemical's environmental hazard potential. Special emphasis is placed on the unique considerations necessary with synthetic organic chemicals in contrast to inorganic chemicals.

INTRODUCTION

Well over 9,000 synthetic organic chemicals are produced in commercial quantities and annually total approximately 140 billion pounds in the United States.(1) Many of these chemicals, such as pesticides, detergents, PCB's and phthalic acid esters, have become well-recognized environmental contaminants. Some of these chemicals are intentionally released into the environment for economic purposes (e.g., pesticides) and others are inadvertently and accidentally released during manufacture, transport, use, and/or disposal. The large number and quantity of organic chemicals being manufactured provides numerous candidates for such releases to the environment. Therefore, a procedure to anticipate future environmental contaminants and to set priorities for environmental research, monitoring and regulatory action is necessary.

Anticipatory action for environmental contaminants is extremely important because of the lag period between the reduction of the release of contaminants to the environment and the reduction of concentrations in the environment. This is especially true of the many lipid soluble organic chemicals which, when incorporated into the food chain, can biomagnify. As an example, one projection indicates that if the use of DDT were decreased to zero by the year 2000, concentrations in the higher levels of the food chain would continue to rise for another decade.(2) Even with a total elimination of DDT use, the concentration in fish would rise slowly for a few years. Thus, by the time a deleterious biological effect caused by a contaminant is noted, years may elapse before corrective action will result in environmental quality improvement. One can envision an environmental thalidomide which might have exceeded the threshold concentration before the effect was realized, and which might take years before remedial action could be effective.

This type of contamination may already be entering the environment. In a review of the water quality information up to 1970, Davis et al.(3) stated that only 66 compounds were identified of the 496 organic chemicals reported to be or suspected to be in fresh water. An EPA laboratory has isolated 34 different non-pesticide synthetic organic chemicals in water at the lower end of the Mississippi River(4), which happens to be a source of drinking water for half the people in the State of Louisiana.

Which of these chemicals or new chemicals coming on the market should be tested first? Which last? Which should be monitored for in the environment? Which should be regulated or banned from the market? A meaningful set of priorities are obviously necessary.

ESTABLISHING PRIORITIES FOR SYNTHETIC ORGANIC CHEMICALS

Assessment of any potential contaminant, whether it is from occupational exposure or environmental sources, requires the consideration of two primary questions (1) at what concentrations does the compound cause any deleterious effects (toxicity) and (2) does the compound reach a biological species in high enough concentration to cause the effect? With environmental contaminants, often the source is quite distant from the biological species being affected which makes the job of assessment much more difficult. However, by reviewing available information on toxicity, production, transport, uses, environmental stability, and the chemistry of the many potentially dangerous compounds, priorities can be set in such a way as to markedly increase the change of identifying environmental hazards.

ENVIRONMENTAL TOXICOLOGY

Perhaps no compounds known can be described as toxic or nontoxic apart from the conditions in which it reacts. Sodium chloride and carbon dioxide, for instance, can be either beneficial or lethal to human life depending on their concentration. Consequently, in defining the toxicity of a given substance, a number of parameters - e.g., concentration, duration and route of exposure, temperature, species, stage of life cycle, etc. - must be defined or at least implied. For most commercial organic chemicals, the toxicity is most often described in terms of acute exposures to man or related mammals, prompted by a concern for industrial safety. For compounds such as pesticides whose use may indicate more direct exposure to man or commercially important animals, chronic toxicity data may also be available. However, more definitive toxicologic information - including studies of carcinogenicity, teratogenicity, and mutagenicity - are often available only for those compounds designed for direct human consumption: drugs, food additives, cosmetics, etc. For example, of the 496 organic chemicals reviewed by Davis et al.(3) only 120 compounds (24%) had been tested for carcinogenicity and only 32 compounds (6%) for teratogenicity. For environmental contaminants, information on chronic and more definitive toxicity is most desirable.

Such detailed toxicity studies are, of course, expensive. A reliable evaluation of chronic toxicity alone has been estimated to cost between $100,000 to $200,000 per chemical.(5) Such costs may often be prohibitive in the development of new and possibly useful chemicals with only marginal or questionable commercial value. Even with the passage of the Toxic Substances Control Act, it is unlikely and may be unreasonable to expect that all of the 300 to 500 new chemicals annually introduced for commercial use(6) will receive anything approaching a complete evaluation of toxicity. However, it is obvious from past experience, that certain chemicals should receive extensive testing regardless of cost. Which compounds will receive such extensive testing should then be dependent on not only the available toxicity data but also a number of more readily described or projected parameters that might be considered under the headings of environmental contamination potential, environmental stability, and probable environmental distribution.

ESTIMATING ENVIRONMENTAL CONTAMINATION POTENTIAL

The potential for accumulation of a chemical in the environment is dependent upon whether it is released to and persists in the environment. Rarely is this information available in quantitative form. Data indicative of release to the environment, such as quantity produced (magnitude of the potential contamination), sites of production, synthesis methods, waste treatment, product uses, are presently available for only a few organic compounds. The U. S. Tariff Commission, which compiles the most comprehensive listing of synthetic organic chemicals(1), only publishes production and sales figures for approximately 10% of the compounds. Other general sources of information include the Chemical Economics Handbook(7) and the Encyclopedia of Chemical Technology(8). These references will provide marketing information on production and use for many but not all of the organic chemicals. When the Toxic Substance Control Act is passed, this type of information will be routinely submitted to EPA.

Correlation of this marketing information into even qualitative estimates of release is one of the least understood and one of the most important factors in determining environmental hazard. Physical properties may provide some insight. Gases and volatile liquids are often released to the environment. Past experience with other known environmental contaminants may also provide some assistance. Nisbet and Sarofim(9) in a study of PCB's routes into the environment concluded that PCB's used as hydraulic fluids, lubricants and heat exchangers provided the major source of water contamination, whereas PCB's used in transformers and capacitors were mainly deposited and mostly retained in land fills (see Table I). Compounds used as detergents or water emulsifiers are known to get out into streams and rivers. As more contaminants are recognized and their sources located, the correlation between marketing data and release to the environment will become more exact.

TABLE I

QUANTITATIVE ESTIMATES OF RATES OF LOSS OF PCBs INTO THE ENVIRONMENT IN 1970 (9)

	Quantity Sold for Use (lbs.)	% of Total Sold	% of Sales Total that was to Replace Discarded PCBs	Quantity Discharged into the Environment (lbs)			
Transformer	13.9×10^6	19	10	1.39×10^6	*** 42.8×10^6 (incineration, open dump or landfill)	36.0×10^6	remained in the dump or landfill
Capacitors	26.7×10^6	37	50	13.35×10^6		6.0×10^6	destroyed by incineration or open burning
Miscellaneous	1.6×10^6	2	~100	1.60×10^6		0.8×10^6	vaporization from open-burn
Plasticizer	19.5×10^6	27	~80-90	16.60×10^6			
			~10-20	2.92×10^6	$2\text{-}4 \times 10^6$	vaporization of plasticizer	
Hydraulic Fluid and Lubricant	7.4×10^6	10	~100	7.40×10^6	$8\text{-}10 \times 10^6$	leaks and disposal of industrial fluids (mostly into fresh and coastal waters)	
Heat Exchangers	4.0×10^6	5	50	2.00×10^6			
Total	73.1×10^6	100	—	45.25×10^6			

***This figure is somewhat higher than the sum of the quantity discharged due to replacement.

ENVIRONMENTAL STABILITY OF ORGANIC CHEMICALS

The importance of environmental stability to setting priorities for potential environmental contaminants is often underestimated. If a compound degrades into innoxious material before it reaches a biological site, its hazard is relatively low. This potential degradation mechanism is especially important with organic chemicals. In contrast, environmental contaminants such as heavy metals may change chemical form (e.g., methylation) or valence state but can not be degraded into innoxious substances such as carbon dioxide and water as can organic chemicals.

Organic chemicals in the environment can be both chemically or biologically altered. However, the most important process contributing to the elimination of organic chemicals from the environment is biodegradation. The action of microbial enzymes generally results in end-products that are entirely inorganic.(10) In contrast, photochemical or other chemical processes in nature usually result in relatively minor alterations of the parent compound, but may provide the slight alteration needed to change a persistent compound to a biodegradable one.

For many years it was felt that the microbial communities of soil and water could destroy any organic compounds which were placed in the environment.(11) Recently, however, it has become evident that microorganisms are not infallible and that some molecules are inherently recalcitrant to microbial degradation.(10, 12) Practical experience with chlorinated pesticides and highly substituted detergents has been especially enlightening. This resistance to biodegradation is dependent not only on chemical structure of the contaminant ["molecular recalcitrance" (12)] but also on the environment (soil, fresh water, marine water, atmosphere, etc.) in which the contaminant comes in contact.

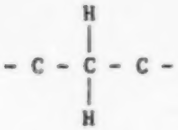
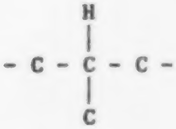
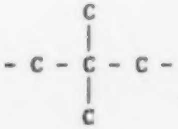
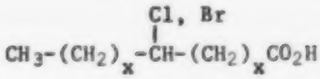
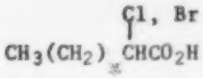
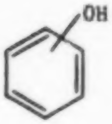
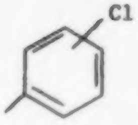
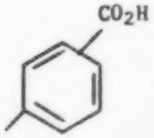
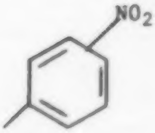
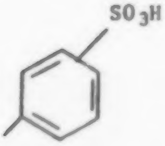
The relationship of chemical structure to biodegradability has been comprehensively reviewed(12-15) and is briefly summarized in Table II. Chemical(16) and photochemical(16-18) reactions in the environment have also been reviewed.

The information available on environmental stability of organic chemicals, which might be used for setting priorities, is rarely very detailed, except when compounds of similar generic structure have been noted as environmental contaminants. Usually a biodegradability test has been run, especially for compounds that might have to pass

TABLE II

Relationship Between Chemical Structure and Biodegradation

Less Persistent ——————————————— More Persistent

Water soluble		Water-insoluble
 $-C-\overset{H}{\underset{H}{\overset{\vert}{\underset{\vert}{C}}}}-C-$	 $-C-\overset{H}{\underset{C}{\overset{\vert}{\underset{\vert}{C}}}}-C-$	 $-C-\overset{C}{\underset{C}{\overset{\vert}{\underset{\vert}{C}}}}-C-$
$R - CH_2OH$ $R - CHO$ $R - CO_2H$ Br, $Cl-CH_2(CH_2)_xCO_2H$	$R-CO_2R$  $CH_3-(CH_2)_x-\overset{\text{Cl, Br}}{\overset{\vert}{C}}H-(CH_2)_xCO_2H$	$R - O - R$  $CH_3(CH_2)_x\overset{\text{Cl, Br}}{\overset{\vert}{C}}HCO_2H$
		
		
		

through a sewage treatment plant. But the difficult task of modelling the laboratory environment to accurately reflect an ecosystem is only too apparent when one compares the test results with the actual environmental behavior of the chemical. However, by combining the available information with the projected chemical structure biodegradability, it is possible to roughly estimate the environmental persistence. Again, with the passage of the Toxic Substances Control Act, information on environmental stability of new compounds will be more systematically generated and hopefully more appropriate to the media to which the compound is released.

ENVIRONMENTAL DISTRIBUTION

Once it is decided that a compound is released to and persists in the environment, it is important, in terms of hazard assessment, to be able to estimate where the chemical might concentrate to dangerous levels in the biological cycles of the environment. Predicting environmental distribution of a contaminant as a diagnostic tool for hazard assessment has some possibilities. However, elemental mercury was considered to be immobile in the environment for many years. Furthermore, Woodwell(19) has suggested that one lesson to be learned from iodine 131 is that "even when the pathways are well understood, it is almost impossible to predict just where toxic substances released into the environment will reach dangerous levels". Using physical properties such as lipid solubility, vapor pressure, and ambient state (gas, liquid, solid) as indicators of bioaccumulation and mobility provides some predictive possibilities. The use of model ecosystems has become quite popular(20), but, for the most part, because of the cost involved, these have been reserved for study of already acknowledged environmental contaminants. However, projection of environmental distribution based on available physical properties, although quite an inexact parameter, can provide some inputs to hazard assessment.

EXAMPLES OF ORGANIC CHEMICAL HAZARD ASSESSMENT

Perhaps the most difficult task in setting priorities is to combine the above parameters in some type of rational fashion. One must first come to the realization that a result based on parameters that are quite inexact will obviously be qualitative, not quantitative.

The complexities involved are best explained by examining some examples. Table III summarizes a great deal of information that was gathered on five general groups of chemicals.(21) All of the chemicals have been produced in sizeable commercial quantities for many years but much of the information that is available is not radically different from what would be available for a new commercial chemical.

Chlorinated naphthalenes provide a good example. The similarity between PCB's and chlorinated naphthalenes in terms of chemical and physical properties and commercial uses is most striking. Both chemicals have been shown to cause chloracne and liver damage in man and many are relatively toxic at low levels. The major differences between the two are the production levels and the uses. In 1970 PCB's were produced in approximately 70 x 10^6 lb a year, although the level has decreased since then. The market for chlorinated naphthalenes is less than 5 x 10^6 lb per year and appears to be decreasing. A major use for both chemicals is as a capacitor impregnate (PCB's - light fixture capacitors, chlorinated naphthalenes - automotive capacitors). However, it is suspected that these capacitors end up in dumps or land fills(9) and since they are contained in a closed system their ability to leach out is relatively low. Formulations used as oil additives, hydraulic fluids, and heat exchanges (PCB's - 11.0 x 10^6 lb, chlorinated naphthalenes - ~1.3 x 10^6 lb) probably have the greatest potential for release to the environment. With chlorinated naphthalenes, the formulation consists of mono- and dichloronaphthalenes which should be much less environmentally persistent. These projections of environmental persistence are based mostly on analogy with PCB's. Only the monochloronaphthalenes have been experimentally tested.

The penta- and hexachloronaphthalene formulation is of some concern. They exhibit high mammalian toxicity, probably are quite persistent, and are used in ways (electroplating stop-off compounds and carbon electrode impregnates) which might lead to environment release. However, they are produced in relatively small quantities (0.4 x 10^6 lb). Thus, although there is some reason to be concerned about chlorinated naphthalenes, they certainly seem to be much less of a problem then were PCB's and can be fairly safely assigned a lower priority than PCB's. Some of the formulations can be assigned an extremely low priority (e.g., the hepta- /octa chloronaphthalenes - low production, relatively low toxicity).

But what about compounds, such as silicones, that have considerably different parameters than chlorinated naphthalenes? The silicone fluids are produced in large quantities (60 x 10^6 lb) and are probably released into the environment in significant amounts from

TABLE III

Factors Effecting the Degree of Potential Environmental Hazard for Selected Compounds (21)

Compound	Production: Recent Annual Production (10^6 lbs)	Production: Rate of Growth	Physical Properties: Physical Form	Physical Properties: Lipid Solubility	Uses	Environmental Persistence	Toxicity			
Chlorinated Naphthalenes (Halowaxes)							Liver necrosis and chloracne in man, plasma Vitamin A reduced			
							Chloracne	TLV	ALD (oral)	Teratogenic, mutagen. carcin. effects
Mono-/Di-	~ 1.3	Stable(?)	Liquid	High	Oil and dye additive	Low-Mod.	Negative	--		--
Tri-/tetra-	~ 2.75	Slowly rising	Solid	High	Auto capacitor impregnate	Mod-High	--	3 mg/m^3		--
Penta-/Hexa-	~ 0.40	Declining (?)	Solid	High	Electroplating carbon electrodes	High	Positive	0.5 mg/m^3	100 mg/rat/dog x 55 days 116 mg/kg b.w. (sheep)	--
Hepta-/Octa-	~ 0.03	Declining (?)	Solid	High	Unknown	High	--	--	1000 mg/rat	--
Silicones (siloxanes)							Chronic pathological effects	LC$_{50}$ ducks	LC$_{50}$ daphnia	Teratogenic, mutagen., carcin. effects
Fluids	60	Rising	Liquid	Med-High	Waxes, polish, cosmetics, emulsions.	High	3 g/kg feed/rat x 2 years - no effect	5 g/kg feed x 8 days	1 mg/1	----
Silicone glycols	18	Rising	Liquid	Med-High	Urethane foams	High	--------	---	500-1000 mg/1	-----
Rubbers (elastomers)	16.6	Rising	Solid (polymer)	-------	Electrical insulation.	High	- ------	---	---	-----
Resins	16.8	Rising	Solid (polymer)	-------	Electrical insulation, paints, and coatings.	High	---------	---	---	Smooth wall tumor after implant
Fluorocarbons							Have caused human death from cardiac arrhythmias (high doses)			
						Residence times	TLV	Death	Cardiac sensit. to epinephrine	Teratogenic, mutagenic, carcinogenic effects
CCl$_3$F	258	6-8%/yr.	Liquid	High	Aerosol propellants	~10 years	5,600 mg/m^3	Negative rat, 10% x 2 hr.	Positive 1.21% x 5 min.	-----
CCl$_2$F$_2$	390		Gas	Med-High	Aerosol propell. & refrigerant	~30 years	4,950 mg/m^3	Negative rat, 20% x 2 hr.	Positive 5.0% x 5 min.	----
CHClF$_2$	80		Gas	Medium	Refrigerant	High	----	Negative rat, 20% x 2 hr.	Positive 5.0% x 5 min.	-----
Cl$_2$C$_2$F$_4$	17		Gas	Medium	Aerosol propellant	High	7,000 mg/m^3	Positive Guinea pigs > 20% x 8 hours	Positive 5.0% x 5 min.	------
Cl$_3$C$_2$F$_3$			Liquid	Medium	Solvents	High	7,600 mg/m^3	Positive rat, 10% x 4 hours		-----
Resins & Elastomers (e.g. Teflon)	16		Solid (Polymer)	-----	Insulation, coatings	High	----	----		-----

TABLE III (continued)

Compound	Production		Physical Properties		Uses	Environmental Persistence	Toxicity				
	Recent Annual Production (10^6 lbs)	Rate of Growth	Physical Form	Lipid Solubility							
Benzenepolycarboxylates							LD$_{50}$ (oral)	intraperit.	inhal.	Teratogenic, mutagenic, carcinogenic effects	
Phthalic anhydride and acid	794	Rising	Solid	Medium	Produce esters for plasticizers. Alkyd resins Synthesis of by-products	Low	2.2 g/Kg mice	1.67 g/Kg mice	30-90 g/1 mice & rats	Negative - (teratogenic)	
Isophthalic acid	95	Rising	Solid	Medium	Alkyd and polyester resins	Low	---	4.2 g/kg mice	-----	------	
Terephthalic acid (& dimethyl ester)	3,321		Solid	Med-High	Polyethylene terephthalate for fiber & films	Low	5 g/kg mice	3.7 g/kg mice	-----	------	
Trimellitic acid & anhydride	11 (esters)		Solid	Med-Low	Produce esters for plasticizers	Low(?)	1.25 - 2.5 g/kg mice	---	-----	------	
Pyromellitic acid	--		Solid	Med-Low	Polyamide polymers	Low(?)	---	---	-----	------	
Chlorophenols							Higher chlorinated phenols can cause liver and kidney damage				
							LD$_{50}$ (oral)	Intraperitoneal	TL$_m$ fish	TLV	Teratogenic, Mutagenic, carcinogenic effects
p-Chlorophenol	> 2	Rising	Solid	Medium	Raw material esp. for 2,4-D P	Low-Med.	500 mg/Kg rat	28/mg/kg rat	14 mg/1	---	----
2,4-Dichlorophenol	53 (as 2,4-D)	Declining	Solid	Med-High	Raw material for 2,4-D	Med.	3600 mg/Kg rat	430 mg/Kg rat	---	---	----
2,4,5-Trichlorophenol	14 (as 2,4,5-T)	Declining	Solid	Med-High	Raw material for 2,4,5-T	Med-High	2460 mg/Kg rat	355 mg/Kg rat	---	---	----
Pentachlorophenol	51	Rising (4%/yr)	Solid	High	Wood preservative	Med-High	135-205 mg/Kg rat	56 mg/Kg rat	.05-.16 ppm	0.5 mg/m^3	----

a variety of uses (e.g., antiforming agents, waxes and polishes). There is good experimental evidence that these compounds are extremely stable in the environment. However, the mammal toxicity data would suggest that these compounds are perhaps one of the more innocuous chemicals ever produced. Some of the fluids are even allowed as food additives. In contrast, one study with daphnia suggests an LC_{30} of 1 ppm.

The silicone rubbers and resins appear to have a very low priority because of their lack of mobility. Their stability suggests that very little material is degraded into compounds that might accumulate in biological systems. Local tissue response to such silicone implants is of medical interest and the phenomena of solid-state carcinogenesis is receiving warranted investigation, but its relationship to environmental hazard is remote at best.

Several questions arise from this comparison. How much should one rely on available toxicological data? How important are production levels? In other words, how should one weigh each of the parameters that are relevant to hazard assessment? The answer is that at this time correlations can only be approximate. However, because of the large numbers of chemicals to be assessed, these approximations will have to be made to allow some numerical assessment. As more experience with both past and present environmental contaminants is gained, these approximations will become more and more exact.

None of the five chemical groups in Table III can be totally eliminated as an environmental hazard, but many formulations can be assigned low risk. Within groups relative risk can more easily be assigned.

The evaluation process clearly provides some research and information needs. A crucial piece of data for chlorinated naphthalenes is whether the penta- and hexachlorinated compounds are released to the environment from their use. By examining the housekeeping practices of the electroplating industry and the carbon electrode manufacturers and users, this question could be easily resolved. Also, some selective monitoring might be in order.

With silicones high priority should be given to clarifying the effects of the compounds on lower organisms and selectively monitoring some environmental samples. One projected use of silicones is as an antitranspirant for plants to reduce losses from the water table. Before this is allowed, a great deal more information on environmental persistence, fate, and effects is needed.

SUMMARY

Assessment of environmental hazard from organic chemicals is possible by reviewing and integrating available information on chemistry, production and use, environmental stability, and toxicity. It is an inexact process subject to error that works fairly well with chemically and commercially related compounds and somewhat less exact with other compounds. However, such reviews are extremely helpful in setting research and data gathering priorities and in identifying high risk hazards. Such assessments should be continuous in order to incorporate new data as it becomes available.

ACKNOWLEDGMENTS

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A LABORATORY MODEL ECOSYSTEM AS AN ELEMENT IN EARLY-WARNING SYSTEMS FOR TOXIC SUBSTANCES

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INTRODUCTION

For the past seven years our laboratory has been studying the development and utilization of a laboratory model ecosystem for the evaluation of the micropollutant potentialities of a variety of synthetic organic compounds. From this work we have evolved a relatively simple and reasonably reproducible terrestrial-aquatic system (Metcalf et al 1971, Metcalf 1972, Metcalf 1974b), and have characterized the degradative fate of more than 70 compounds including organochlorine, organophosphorus, and carbamate insecticides, insect growth regulators, herbicides, fungicides, toxic impurities and degradation products such as DDE, photodieldrin, and tetrachlorodibenzodioxin, industrial chemicals such as PCB's and phthalate plasticizers, important heavy organic chemicals, and of lead and cadmium [Kapoor et al. (1970), (1971), (1973); Hirwe et al. (1972); Metcalf et al. (1973 a,b,); Metcalf and Lu (1973); and Metcalf (1974b)]. This model ecosystem methodology has been widely imitated elsewhere and has been selected by the World Health Organization as a standard test method for evaluating the environmental impact of new candidate pesticides for vector control uses in aquatic situations [Metcalf (1974a)]. The system is presently being used by the Illinois Natural History Survey to evaluate the potential environmental impact of all new agricultural chemicals intended for use in Illinois. In our laboratory, we have found the model ecosystem to be a valuable tool for basic studies of the principles of biodegradability using the DDT-type compound as a model [Kapoor et al. (1970), (1971), (1973); Metcalf et al. (1973); Metcalf (1974b); Coats et al. (1974)].

From these investigations it appears that this type of laboratory model ecosystem has at least the following major uses:

1. Screening of new candidate pesticides for environmental toxicity to a variety of organisms, to

determine pathways of environmental degradation, and to characterize quantitatively bioaccumulation and biodegradability.

2. Evaluation of the suitability of various pesticides for specific uses involving environmental contamination, e.g., larvicides for application to streams, lakes, and reservoirs where fish culture is important.
3. Evaluation of the pollutant potential of various synthetic chemicals which may enter into the aquatic environment as trace contaminants from use or manufacturing effluent.

METHODS

The model ecosystem technology has been fully described [Metcalf et al. (1971); Metcalf (1974b)]. The entire evaluation is based about the use of radiolabeled molecules which permits tracing the parent compound and its degradation products through the various organisms and food chains of the system and the quantitative determination of the amounts stored in the various organisms. Radiolabeled degradation products are extracted from various organisms of the model ecosystem, separated by thin-layer chromatography (TLC) on silica gel, and visualized by radioautography on X-ray film for ^{14}C, ^{35}S, or ^{32}P-labeled compounds (Figure 1) or by serial scintillation counting for ^{3}H-labeled compounds. The individual components are then characterized both quantitatively by direct liquid-scintillation counting and qualitatively by cochromatography with known model compounds, by appropriate microchemical reactions, and by infrared, mass, and nmr spectrometry. The use of silica gel containing fluorescent ZnS is especially helpful in visualizing the location of various model compounds on TLC chromatograms.

^{14}C and ^{32}P labeled compounds have been obtained from various commercial suppliers, from the manufacturers of specific products, or synthesized in our laboratory. A sample and inexpensive method for ^{3}H-labeling of aromatic compounds [Hilton and O'Brien (1964)], used in conjunction with the Schöniger Oxygen Flask combustion technique [Kelly et al. (1961)], has been very useful.

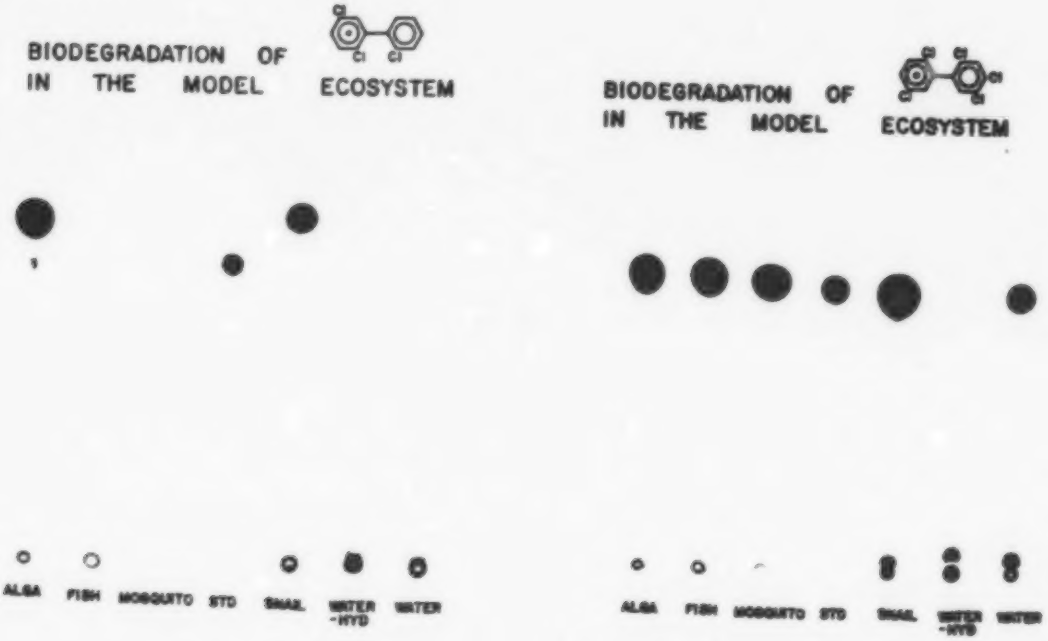

FIGURE 1. RADIOAUTOGRAMS OF TLC PLATES SHOWING DEGRADATION OF TRICHLORO- AND PENTACHLORO-BIPHENYLS IN LABORATORY MODEL ECOSYSTEM

[From Metcalf and Lu 1973)]

Laboratory Model Ecosystem

The system as developed after several years of study is shown in Figure 2. It consists of a 25 x 30 x 45-cm glass aquarium containing a sloping shelf of washed white sand. The lower portion is covered with 7.1 of standard reference water [Freeman (1953)] which provides satisfactory mineral nutriation for the growth of Sorghum vulgare on the 15-cm flattened terrestrial portion, and for the filamentous alga Oedogonium cardiacum in the aquatic portion. The latter is seeded with a complement of plankton (diatoms, protozoa, rotifera), 30 Daphnia magna, and 10 Physa snails. The aquarium is provided with aeration and placed in an environmental plant growth chamber at 80°F (26°C) with 12-hour simulated daylight of 5000 ftc (54,000 lux). A Plexiglas cover, 28 x 30 cm covers the aquatic portion of the chamber and reduces evaporation.

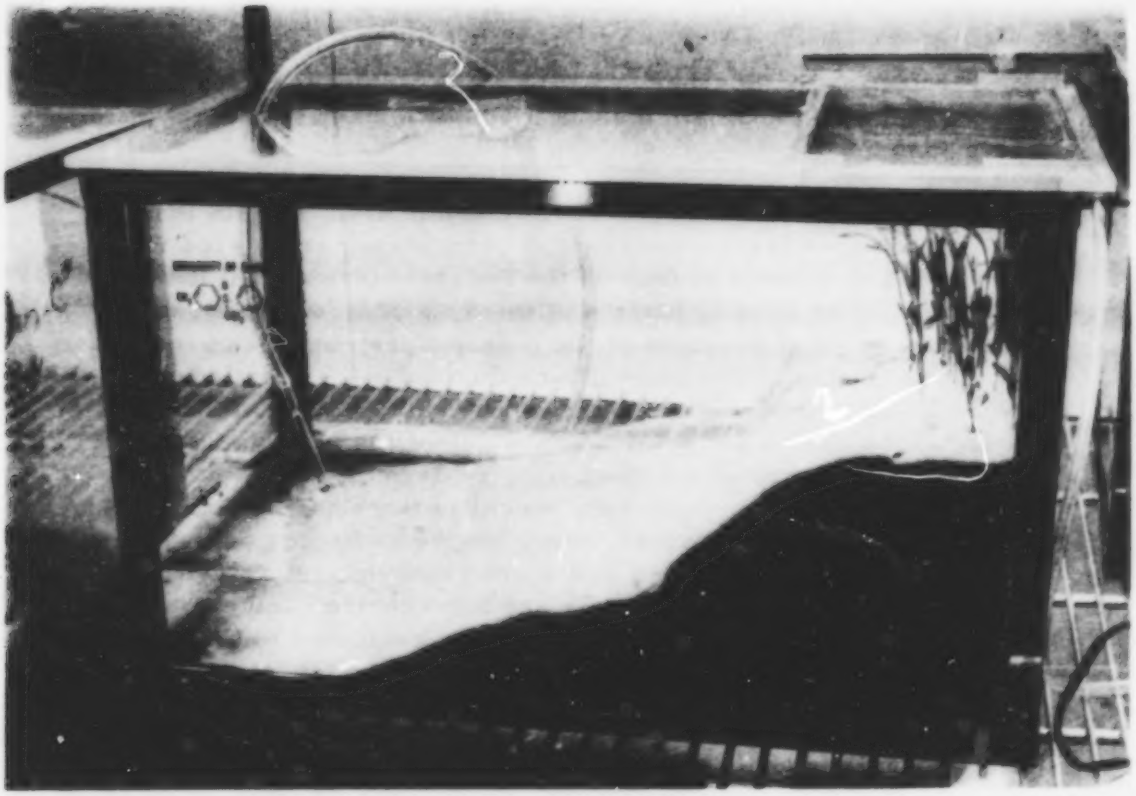

FIGURE 2. LABORATORY MODEL ECOSYSTEM USED IN EARLY-WARNING STUDIES

[From Metcalf et al. (1972)]

For operation of the model ecosystem 50 Sorghum seeds (Pioneer 846) are planted in 5 rows on the flat terrestrial portion and the aquarium allowed to equilibrate about 20 days when the plants are about 15 cm high. Radiolabeled pesticides for investigation are typically applied at 1 mg to 5 mg/chamber (0.2 to 1 lb/A) dissolved in about 0.3 ml of acetone and quantitatively applied to the leaves with a capillary pipette. As useful alternatives, the radiolabeled compound can be applied as a seed treatment, as a soil treatment by injecting 50 x 5 μl amounts with a micrometer-driven syringe, pipetted directly into the water phase, applied as a spray of aerosol, or mixed with standard soils and incorporated into the sand phase before planting the *Sorghum*. All of these techniques have been used to give valuable information about distribution and fate of materials under test.

At an appropriate interval after application, ten 4th instar *Estigmene acrea* larvae (salt marsh caterpillar) are placed in the aquarium and allowed to feed on the *Sorghum* plants until these are consumed. The aquatic portion of the aquarium is subsequently contaminated by fecal products of the caterpillars, by bits of leaf frass, and by the bodies of the caterpillars themselves – simulating natural channels of contaminant transport. The radiolabeled products enter various food chains and after 26 days, 300 *Culex quinquefasciatus* mosquito larvae are added, and after 30 days, three *Gambusia affinis* fish. Typically, the experiment is terminated 33 days after application of the radiotracer, when weighed samples of fish, snails, mosquito larvae, algae, and water are removed and assayed for total radioactivity. The samples are homogenized and extraced with acetonitrile and the concentrated extracts examined by TLC (Figure 1). The unextractable radioactivity from the various substrates is determined by combustion analysis in the Schöniger oxygen flasks.

Evaluation of Results. A standard methodology has been developed to compare the model ecosystem results for the various contaminants. The concentrations of total radiolabel and that of each of the components separable by TLC is determined in ppm. These are arranged in standard tabular form to permit easy determination of two important parameters: (1) the *ecological magnification* (E.M.) or ratio of concentration of parent radiolabeled compound (or of any key degradation product) in fish, snail, mosquito, daphnia, or alga to concentration in water; and (2) *biodegradability index* (B.I.), a numerical method for evaluating the relative biodegradability of any candidate compound, defined as the ratio of radiolabeled polar compound to the radiolabeled non-polar compounds, in fish or other organisms. The data for determining this parameter are readily obtainable from TLC separations of the extracts, using a nonpolar solvent such as hexane or ether-hexane mixture. The polar materials remain at the origin while the non-polar compounds move up the TLC plate as shown in Figure 1. B.I. values for various compounds have ranged from 0.0001 to >1000 and examples are shown in Tables 1, 2 and 3.

The *unextractable radioactivity* in the various organisms is a measure of total degradation of the test compound and has varied from as low as 0.1% for DDE to as high as 60% for various highly degradable

TABLE 1. SUMMARY OF MODEL ECOSYSTEM EVALUATION OF ^{14}C POLYCHLORINATED BIPHENYLS

From Metcalf and Lu (1973)

	2,5,2'-tri-chlorobiphenyl	2,5,2',5'-tetra-chlorobiphenyl	2,5,2',4',5 -penta-chlorobiphenyl
Concentration in fish, ppm	1.28	14.23	119.70
Unextractable radio-activity, %	14.6	2.4	1.1
Ecological magnification	6,400	11,863	12,153
Biodegradability index	0.60	0.060	0.019

TABLE 2. DEGRADATION OF 2,3,7,8-TETRACHLORODIBENZO-p-DIOXIN (TCBD) IN MODEL ECOSYSTEM

	TCBD Equivalents, ppm					
	H_2O	Oedogonium (alga)	Daphnia (daphnia)	Physa (snail)	Culex (mosquito)	Gambusia (fish)
Total ^{14}C	0.00144	0.825	1.338	1.358	1.895	0.178
TCBD (R_f 0.62*)	0.00034	0.825	1.256	1.256	1.837	0.17
Unknown (R_f 0.06)	0.000039	--	--	0.0644	--	--
Polar (R_f 0.0)	0.00036	--	--	0.0380	--	--
Unextractable	0.0007	0.134	--	0.142	0.0578	0.074

*TLC with hexane (Skellysolve B b.p. 60-68 C)
E.M. fish 500, snail 3694
B.I. fish 0.001, snail 0.029.

TABLE 3. DEGRADATION OF α-TRICHLOROMETHYL-p-ETHOXY BENZYL-p-ETHOXYANILINE IN MODEL ECOSYSTEM

From Hirwe et al. (1972)

	Equivalents, ppm				
	H_2O	Oedogonium (alga)	Physa (snail)	Culex (mosquito)	Gambusia (fish)
Total ^3H	0, 363	3, 03	36, 0	1, 0	0, 30
$C_2H_5OC_6H_4NHCH(CCl_3)C_6H_4OC_2H_5$	0, 055	1, 09	22, 68	0, 28	0, 041
$C_2H_5OC_6H_4NHCH(CCl_3)C_6H_4OH$	0, 031	0, 43	2, 02	0, 13	0, 081
$HOC_6H_4NHCH(CCl_3)C_6H_4OH$	--	--	1, 512	--	0, 03
$C_2H_5OC_6H_4C(O)CHCl_2$	--	0, 3	3, 542	--	0, 028
$C_2H_5OC_6H_4NH$	0, 053	0, 42	2, 556	0, 01	0, 03
$C_2H_5OC_6H_4C(O)OH$	0, 123	0, 38	1, 800	0, 06	0, 03
Unknown (R_f 0, 4)*	0, 053	--	--	0, 15	--
Polar (R_f 0, 0)	0, 042	0, 40	2, 520	0, 22	0, 060

*TLC with ether-petroleum ether (b. p. 60-68 C) (1:1)
E. M. snail 418, fish 0, 75
B. I. snail 0, 075, fish 0, 25

compounds whose radioactive-label becomes incorporated in the total metabolic pool.

Degradative pathways describing the environmental fate of the test compound can be determined after identification of the majority of the key degradation products as shown in Figure 3.

Environmental toxicity to any of the various organisms in the model system is easily observed, and can be related to water concentration of parent compound, as measured at intervals during the course of the experiment. When all the organisms are killed as occurred with the pesticide endrin which at 2 ppb killed all the fish, these are restocked at intervals until survival occurs, thus giving an early warning of potential toxic hazard [Metcalf et al. (1937b)].

Other calculations which can be made include the total biomass concentration of test compound and its degradation products in each of the organisms, the rate of uptake of radiolabeled products from water by the various organisms, and the nature of consecutive

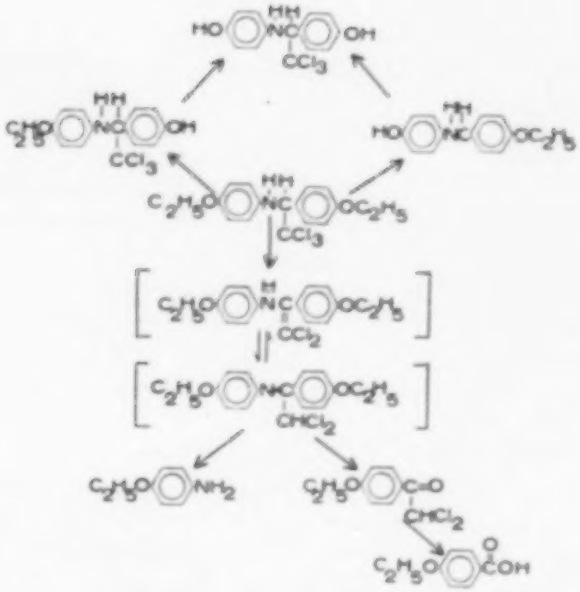

FIGURE 3. DEGRADATIVE PATHWAYS FOR α-TRICHLOROMETHYL-p-ETHOXYBENZYL-p-ETHOXYANILINE IN LABORATORY MODEL ECOSYSTEM

[From Hirwe et al.(1972)]

environmental reactions occurring in the water phase as determined by TLC evaluation of the relative amounts of various products in the water at regular intervals during the course of the experiment.

RESULTS

Screening of New Candidate Pesticides

The model ecosystem has been used extensively in our laboratory to screen a variety of analogues of DDT for environmental degradability. These compounds were synthesized as part of a long term project to determine if it was feasible to produce insecticides which might be persistent on inert surfaces yet relatively biodegradable when absorbed by living organisms. The basic methodology involved systematic study of the DDT molecule by replacing the environmentally stable C-Cl bonds with other isosteric groups which could serve as degradophores by acting as substrates for the mixed function oxidases [Metcalf et al. (1971), (1972)]. The action of the detoxifying enzymes on molecular moieties which could serve as substrates was shown to result in substantial changes in the polarity of the molecule so that the degradation products were excreted rather than stored in lipids as is the principal problem with DDT. In order for candidate insecticidal compounds to have appropriate biological activity there is also a precise requirement for molecular size and shape to be bioisosteric with DDT.

The model ecosystem has been used to characterize the biodegradability and degradation pathways of some of the most promising of these DDT-substitutes using ^3H and ^{14}C-radiolabeled compounds [Kapoor et al. (1970), (1971), (1973); Metcalf et al. (1971); Coats et al. (1974); Hirwe et al. (1974)].

The model ecosystem evaluation of the various DDT analogues produced some interesting surprises as shown in Table 4. Methoxychlor ($R_1=R_2=CH_3$) and ethoxychlor ($R_1=R_2=C_2H_5O$) were substantially biodegradable in fish but not in snail. Their primary degradation was by O-dealkylation to mono- and bis-phenols [Kapoor et al. (1970), (1971)]. Methylchlor ($R_1=R_2=CH_3$) was highly biodegradable in fish but poorly degradable in the snail and was degraded by R-CH_3 oxidation to mono- and bis-carboxy acids [Kapoor et al. (1971)]. Methiochlor ($R_1=R_2=CH_3S$) was the most readily degradable compound studied and was rapidly oxidized in vivo to a mixture of sulfoxide and sulfone derivatives [Kapoor et al. (1970)]. The compounds with asymmetric aryl substituents were substantially degradable in fish and less so in snail [Kapoor et al. (1973)]. Chloro-methylchlor ($R_1=Cl$, $R_2=CH_3$) was intermediate in degradative behavior between DDT and methylchlor showing the importance of a single degradaphore group in promoting excretion rather than lipid storage. Methyl ethoxychlor ($R_1=CH_3$, $R_2=C_2H_5O$) was highly degradable in fish and was excreted through two pathways involving oxidation to carboxylic acid and O-deethylation to phenol.

Systematic examination of DDT analogues with altered aliphatic moieties is still in progress. However dianisyl neopentane ($R_1=R_2=CH_3O$, $R_3=C(CH_3)_3$ a methoxychlor isostere was scarcely anymore degradable than methoxychlor and was degraded very

TABLE 4. MODEL ECOSYSTEM CHARACTERIZATION OF BIODEGRADABILITY OF DDT ANALOGUES[(a)]

R_1	R_2	R_3	EM[(b)] Fish	EM[(b)] Snail	EM[(c)] Fish	EM[(c)] Snail
Cl	Cl	CCl_3	84,500	34,500	0.015	0.045
Cl	Cl	$HCCl_2$	83,500	8,250	0.054	0.24
CH_3O	CH_3O	CCl_3	1,545	120,000	0.94	0.13
C_2H_5O	C_2H_5O	CCl_3	1,536	97,645	2.69	0.39
CH_3	CH_3	CCl_3	140	120,270	7.14	0.08
CH_3S	CH_3S	CCl_3	5.5	300	47	0.77
Cl	CH_3	CCl_3	1,400	21,000	3.43	2.0
CH_3	C_2H_5O	CCl_3	400	42,000	1.20	0.25
CH_3O	CH_3S	CCl_3	310	3,400	2.75	105
CH_3O	CH_3O	$C(CH_3)_3$	1,636	23,000	1.04	0.23
Cl	Cl	$HC(CH_3)NO_2$	125	33,231	7.38	0.034

(a) Data from Metcalf et al. (1971), Kapoor et al. (1973), Coats et al. (1974), Hirwe et al. (1974).

(b) Ratio of concentration in organism/concentration in water.

(c) Ratio of polar/nonpolar metabolites.

largely through O-demethylation to mono- and bis-phenols rather than by enzymatic attack on the neopentyl group [Coats et al. (1974)]. These neopentyl analogues have been suggested as non-chlorine substitutes for DDT and this kind of quantitative model ecosystem data is a good example of the early warning potentialities of model ecosystem evaluation.

Prolan® the nitropropyl analogue of DDT (R_1=R_2=Cl, R_3=$HC(CH_3)NO_2$) showed surprisingly little concentration in fish and was degraded exclusively through attack on the aliphatic moiety largely by dehydronitrification and oxidation to 4, 4'-dichlorodiphenyl acetic acid [Hirwe et al. (1974)]. Thus it appears possible to produce substantially degradable DDT-type analogues by altering only the aliphatic moiety. From these model ecosystem studies of DDT analogues it seems apparent that there are a number of DDT-type compounds whose use is much more compatible with environmental quality than that of DDT itself.

Suitability of Insecticides for Vector Control

The World Health Organization (WHO) has the responsibility for technical guidance of control programs for vectors of human diseases. A new program is being developed in tropical Africa for the curbing of the filarial disease of humans, onchocerciasis. This disease caused by *Onchocerca volvulus*, affects more than 20 million people of whom 20% or more may become blind [WHO (1973)] because of the parasitic worms' invasion of the eye. Onchocerciasis is transmitted between humans by the black flies *Simulium* which breed as larvae in running water. Thus the disease is concentrated along fertile river valleys and is increased with irrigation projects. In an "all out" attack on this disease in the Volta River basin of West Africa, the use of DDT was first proposed as a *Simulium* larvicide. Actually, DDT is not especially effective against black fly larvae and its wide use by aerial spraying is incompatible with environmental quality. A WHO laboratory screening program selected a number of candidate larvicides among which chlorpyrifos *O*,*O*-diethyl *O*-(3,5,6-trichloro-2-pyridyl) phosphorothionate (OMS 971 or Dursban®) was the most effective. However the corresponding *O*,*O*-dimethyl ester (OMS 1155) was almost as effective as a larvicide and much less toxic to man and higher animals. As part of the selection criteria, the relative environmental degradability of the two esters was evaluated using 3,5,6-trichloro-2-pyridyl -^{14}C-2,6- labeled phosphorothionate esters in the model ecosystem. The results [Metcalf (1974b)] provided an excellent example of the utility of the model ecosystem as an early warning system. The comparable values for chlorpyrifos and chlorpyrifos methyl are shown below:

	Chlorpyrifos	Chlorpyrifos Methyl
Parent compound in fish, ppm	0.0352	0.0076
Unextractable ^{14}C, %	23.9	52.2
Ecological magnification	314	95
Biodegradability index	1.02	3.95

Chlorpyrifos methyl is evidently substantially more biodegradable and less accumulative in the fish, *Gambusia* than chlorpyrifos. On the basis of its lower toxicity and higher biodegradability chlorpyrifos methyl was selected as the more suitable larvacide for Simulium control [Quellennec (1972)]. Comparison of the values above with those of DDT and methoxychlor (Table 1) will indicate the importance of the increased biodegradability of these organophosphorus insecticides. Similar model ecosystems are being made with other pesticides proposed for use in WHO programs.

Polychlorinated Biphenyls (PCB's)

These industrial compounds have become almost as ubiquitous in the environment as DDT and like DDT and DDE have been found to be biomagnified in tissues of fish and other animals to levels as 10^7 fold. These residues may pose a severe hazard to the reproductive capacities of animals, e.g., mink, and have been shown to cause teratogenesis [Envir. Health Persps., No. 1 (1972)]. The problems of PCB pollution of the environment are greatly complicated by the large number of individual chemical components of each industrial fraction, i.e., Arochlor 1242 (42% chlorine) has at least 30 isomeric chlorobiphenyls. To make critical judgments of the severity of environmental effects from these various compounds, these ^{14}C-ring labeled chlorinated biphenyls were evaluated in the model ecosystem [Metcalf and Lu (1973)]. A summary of the results is given in Table 1.

The model ecosystem results clearly show that the environmental hazard increases with the number of chlorine atoms in the biphenyl nucleus and that the biphenyls containing higher percentages of chlorine may be expected to persist longer in nature and to accumulate to higher levels.

Endrin

The use of ^{14}C-ring labeled endrin or 1,2,3,4,10,10-hexachloro-6,7-epoxy-1,4,4a, 5,6,7,8,8a-octohydro 1,4-*endo*, *endo*-5,8-dimethanonaphthalene (2.3 m Ci/mmole) in the model ecosystem provided a good example of early-warning potentialities. Endrin was applied at 1.0 mg (0.2 lb/A) or 0.2 the usual application rate in model ecosystem investigations. Biological observations of the organisms in the system were particularly informative. The compound was highly toxic to the salt marsh caterpillar even at the reduced dosage. As the level of contamination in the water rose to 0.06 ppm the Daphnia and Culex larvae were repeatedly killed and had to be reintroduced. The water phase was incredibly toxic to Gambusia developed violent convulsions within a few minutes of being placed in the aquarium and died within a few hours. This water toxicity persisted for more than 60 days from the beginning of the experiment and was associated with water concentrations of endrin from 1-2 ppb. This toxicity delayed the termination of the experiment for twice the usual 33 day period and provided a striking parallel to the Mississippi River fish kills associated with endrin wastes [Barthel et al. (1969)]. Thus this experiment demonstrated the predictive value of the biological observations.

At the conclusion of the experiment, endrin was present in the organisms of the system: *Oedogonium* 11.56 ppm (84.9% total ^{14}C), *Physa* 125.0 ppm (82.8%), and *Gambusia* 3.40 ppm (75.8%). The degradation products were apparently heto- and hydroxy- derivatives. The E.M. values were fish 1335 and snail 49,218, and the B.I. values were fish 0.009 and snail 0.0124 [Metcalf et al. (1973)].

TCBD

This compound 2,3,7,8-tetrachlorodibenzo-*p*-dioxin (ring UL-^{14}C, 0.64 in Ci/mmole) was found to be highly persistent in the model ecosystem as shown in Table 2 [Metcalf et al. (1974)]. The intact TCBD comprised from 93 to 99% of the extractable ^{14}C in the various organisms, with only traces of an unknown degradation product (R_f 0.06) appearing in the snail and in the water. At the conclusion of the experiment, the TCBD level in the water was 0.34 ppb or at the water solubility level. The E.M. values ranged from 500 in fish to 5574 in *Culex* larvae, and the B.I. values from about 0.001 in fish to 0.08 in snail (Table 2). These model ecosystem data together with the extreme toxicity and teratogenicity of TCBD (Envir. Health Persp. No. 5, 1973) and its metabolic stability (Vinopal and Casida 1973) give strong early warning signals that this toxic impurity formed in the manufacture of chlorinated phenols cannot be tolerated as an environmental pollutant in any detectable amounts.

An Environmental Unknown

To explore further the value of the model ecosystem technology as an early warning, we will consider an environmental unknown, a potential new candidate insecticide α-trichloromethyl-*p*-ethoxybenzyl-*p*-ethoxyaniline (Hirwe et al., 1972). This compound was ^{3}H-ring labeled at 1.2 mCi/mmole and evaluated in the model ecosystem in the usual manner with the results shown in Table 3. The compound is degraded to more polar metabolites by O-dealkylation to form mono- and bis-phenols. It also undergoes a dehydrochlorination followed by a tautomeric shift to an unstable intermediate α-dichloromethyl-p-ethoxybenzylidine-p-ethoxyaniline which is cleaved to p-ethoxyaniline and p-ethoxydichloro-acetophenone. (Figure 3). The latter, identified by mass spectrometry, is further degraded to p-ethoxybenzoic acid. Other products which must form but were not identified are the easily conjugated p-hydroxyaniline and p-hydroxybenzoic acid. The parent compound was substantially concentrated in the snail, E.M. 418, but not in the fish, E.M. 0.75. The values for B.I. were snail 0.075 and fish 0.25. However, these depend on the definition of polar metabolites and the values given represent a conservative view. From this evidence, the reader may draw his own conclusions about the potential effects of this compound on environmental quality.

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METHODS FOR DETECTION OF TERATOGENIC AGENTS

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ABSTRACT

Current methods used for detection of teratogenic agents consist of three defense systems: (1) animal testing and prediction from chemical structure, (2) in vitro testing by tissue culture, organ culture, or whole embryo culture, and (3) monitoring at the fetal, new born and later periods. Since experience shows that all too often the last of the three defenses, the monitoring systems, must be used, there is an urgent need to make the testing systems more reliable.

THE WORLD HEALTH ORGANIZATION'S ENVIRONMENTAL HEALTH CRITERIA AND AIR MONITORING PROGRAMS

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INTRODUCTION

The World Health Organization is the intergovernmental organization of the UN system dealing with health. WHO was established in 1948; it now has 135 member states, whose constitutional bodies are the World Health Assembly, which meets once every year, and the Executive Board. The Organization is headed by the Director General, who is elected by the World Health Assembly. It has its headquarters in Geneva and has six Regional offices, namely, in Washington, D.C. for the Americas (united with the Pan-American Health Organization), in Copenhagen for Europe, in Brazzaville for Africa, in Alexandria for the Middle East, in New Delhi for Southeast Asia, and in Manila for the Western Pacific. Its total staff is about 5,000 people and its working budget in 1973 was just over U.S. $90 million.

The objective of WHO is the attainment by all people of the highest possible level of health.

It should be clearly understood that WHO functions largely as an advisory body.

Concern over the human environment is a constitutional function of the World Health Organization. Enviornmental health was therefore one of the five priorities established for WHO's program of work at the First World Health Assembly in 1948. Following an in-depth review, the Twenty-fourth World Health Assembly in 1971 adopted as part of its fifth General Program of Work for the specific period from 1973-1977, inclusive, that the promotion of environmental health remain one of the principal program objectives of the Organization next to the strengthening of health services, the development of health manpower, and disease prevention and control. The program includes assistance to countries for: the provision of basic sanitary services as a continuing activity for the control of communicable diseases; the control of environmental pollution and nuisances as a means of protecting health and ov avoiding disturbances in the ecological systems; the improvement of environmental conditions in urban and industrial areas; and the provision of the necessary infrastructure, including manpower, to carry out effective environmental health programs. It should generate technical information regarding environmental health conditions, such as maximal permissable levels of pollutants in air, water, soil, and food, and should assist countries in developing national systems for gathering such information and for determining when and where preventive action is required. This should facilitate the formulation of environmental health criteria in relation to food technology, pollution, environmental radiation, noise and other nuisances, and to occupational exposure of workers, as a basis for the establishment of national standards.

As the International Reference Center for Air Pollution Control of the WHO, the NERC/RTP is directly participating in and providing the lead role for the WHO Environmental Criteria Program and Air Monitoring Program.

WHO ENVIRONMENTAL HEALTH CRITERIA PROGRAM

WHO defines environmental health criteria as the quantitative relations between the exposure to a pollutant and the risk or magnitude of an undesirable effect under specified circumstances defined by environmental variables and target variables. In WHO's view, environmental health criteria are basic tools for action against pollution, for the planning of programs, for the setting of national standards, and for the evaluation of environmental programs.

It should be made clear that WHO environmental health criteria are essentially scientific information which are hoped to become input into national endeavors. In other words, it is not WHO policy to develop universal derived working limits, universal air quality standards, etcetera. They do believe, however, in the universality of scientific information. Therefore, the prime objective of the WHO environmental health criteria program is to promote agreement among the scientists on scientific information related to the quantitative relations between exposure to pollutants and the risks and on accepted maximum levels of a pollutant in the organism or the population.

Environmental health criteria pollutants were prioritized on the basis of: the severity of adverse effects on the population; the persistence of the agent in the environment; metabolic degradation or synthesis in biological systems; the ubiquity and abundance of the agents in man's environment; the size, type, and demographic characteristics of the population exposed as well as work done in the past; the feasibility of control and prevention; the degree of control that already exists; the extent of knowledge available; and many other considerations.

Obviously, any ordering of priorities will receive continuous review. Notwithstanding, however, there was agreement that an initial series of environmental factors be considered for immediate examination, namely:

1. Oxides of nitrogen (NO_x), because of their unclear public health implications in the ambient air;

2. Mycotoxins, because of their possible contribution to chronic disease, including cancer, especially in the largely agricultural countries with warm and damp climates;

3. Nitrates and nitrites, because of the possibility of ultimate conversion to nitrosamines in man, and the use of nitrates in agriculture and of nitrites in food;

4. Manganese, because of its demonstrated neutrotoxicity and the possibility of its becoming more widely disseminated primarily as a fuel additive;

5. Polychlorinated biphenyls (PCBs), because of their demonstrated persistance, toxicity and wide dissemination in water, packaging material and paints;

6. Asbestos, because of its demonstrated carcinogenic properties and widespread use for industrial, structural and other commercial purposes.

What now is the machinery which WHO apply in establishing environmental health criteria?

Three different procedures are envisaged:

A. Preparation of new criteria documents. This will be carried out in three stages:

   (i) Preparation of an outline for national contributions and preparation of national contributions.

   (ii) Consolidation of national contributions into draft criteria documents. This will be done on sub-contract either to individual experts or to WHO Collaborating Institutions.

   (iii) Review of the draft by task groups of international experts.

The total time estimated for the preparation of such documents is about 18 months from the moment the outlines are circulated to national institutions.

B. Preparation of criteria documents based on existing documentation. This approach will be used where criteria-like documents (either WHO or national) already exist. The following stages are envisaged:

   (i) Preparation of a draft criteria document based on an outline established by the WHO secretariat. This work will be done on a contract with recognized experts.

   (ii) Circulation of the draft document to national institutions for comments and additions.

   (iii) Revision of the draft document based on national comments. This will be done as a part of the contract under (i).

   (iv) Review of the final draft document by task groups of international experts. Total estimated time for for the preparation of a document is 12 to 14 months.

C. Preliminary reviews. As recommended by the Secretary General's Report, a short-cut procedure is envisaged consisting only of two stages:

(i) Preparation of a draft preliminary review according to an outline established by the WHO secretariat. This will be done on contract with recognized experts in the field.

(ii) Review of this draft by task groups of international experts. Estimated time for the preparation of a preliminary review is 6 to 8 months.

The environmental pollutants scheduled for consideration during the period 1973-1975 are listed in Table 1 according to the respective procedural approach.

TABLE 1. ENVIRONMENTAL HEALTH CRITERIA POLLUTANTS PROCEDURE

Group	A	B	C
I	Mn; Nitrates, nitrites, nitrosamines; PCBs; Mycotoxins	Cd; Hg; Pb; NO_x; asbestos	Sb; Bi; Se; Mo; Te; Ti; Ge; Sn; Organic dusts; Petroleum Products
II	Ni; V; Sulfates-H_2SO_4 aerosols; Fluorides; Chlorinated bioacides and chlorine	As; Be; Cr; SO_2 and suspended particulate matter; CO; Ozone and oxidants; polycyclic hydrocarbons	Li; Ba; La; Al; Ga; Zn; Fe; Ni; Co; Pd; Pt; Inert dusts; Plastics

WHO AIR MONITORING PROGRAM

The WHO program to assist Member Countries in establishing, developing, and operating air pollution monitoring networks was initiated toward the end of 1967. The program is implemented through the WHO reference centers and collaborating laboratories on air pollution, which include, at present, two International Reference Centers (IRC), the IRC for Clinical and Epidemiological Aspects of Air Pollution at the Medical Research Council's Air Pollution Unit, St. Bartholomew's Hospital Medical College, London; and the IRC on Air Pollution Control at the Environmental Protection Agency, Washington, D. C., United States of America. In addition, there are three regional reference centers at Moscow, Nagpur, and Tokyo; seven national reference centers and eleven collaborating laboratories; plus laboratories in 19 cities in the Pan American Sampling Network.

One of the main functions of the reference centers and collaborating laboratories is to promote the use of uniform methods of measurement; to introduce reliable and effective procedures for the calibration of routine sampling and analytical methods; to improve the quality of monitoring systems; and to standardize the handling, statistical analysis, and use of data. This program will also help in generating internationally comparable data on levels and trends of air pollution in some urban and industrial areas; these comparable data may help in identifying patterns of exposure to air pollution; may facilitate the planning and assessment of health effects studies carried out in different countries; and may facilitate the comparative evaluation of the effectiveness of national air pollution control programs--to mention only some of the uses of such information.

As a part of the program, a number of monographs on the measurement of common air pollutants have been prepared and distributed to the collaborating laboratories and national reference centers for use and comments.

WHO recently initiated a pilot study to evaluate and test a scheme for handling and statistically analyzing air pollution data. Forty-eight sites located within 16 countries are involved in this pilot study. The pollutants monitored in the study are confined to SO_2 and suspended particulate matter. Each country selected three sites within a major city, one from each of the three categories, "inner city - commercial", "inner city - industrial", and "suburban - residential", in order to be representative of existing concentrations throughout the city.

The countries that agreed to participate in this activity are: Austria, Belgium, Canada, Czechoslovakia, Federal Republic of Germany, India, Israel, Italy, Japan, The Netherlands, Spain, Sweden, United Kingdom, USSR, Yogoslavia, and the United States.

It was recently recommended at a joint meeting that the monitoring network operations be expanded to:

a. Increase the number of sampling stations per country up to 8;

b. Increase the number of countries to 30; and

c. Increase the number of pollutants measured. The next pollutant for consideration would be ozone.

WHO ENVIRONMENTAL HEALTH MONITORING PROGRAM

Introduction

The United Nations Conference on the Human Environment (Stockholm, 1972) adopted several recommendations (Nos. 71, 73, 77, 78, and 82) that directed WHO and other international organizations to develop programs for monitoring the levels of pollutants in air, food and water and to use the information derived from such activities, and from other sources, to develop criteria and standards for the protection of human health. In fact, monitoring activities recommended by the Stockholm Conference are part of a comprehensive Earthwatch program, the function of which will be (a) monitoring, (b) evaluation of, (c) research, and (d) exchange of information on the state of the environment as a basis for rational environmental management decisions, and for an early warning of possible major effects harmful to man's health and well-being.

The objectives of the proposed program are:

1. To strengthen national environmental and health monitoring systems and
2. To provide an international information synthesis on trends and levels of environmental quality and its effects on man's health and well-being, based on selected data provided by national monitoring systems.

Priorities

1. Technical assistance

   The provision of technical assistance to national monitoring systems is the major component of the program.

2. International Information synthesis

   An international synthesis of environmental health data supplied by national monitoring systems can be attempted only if such data are comparable and if the monitoring systems are designed so as to enable a meaningful interpretation of data.

A computerized inventory will have to be maintained of relevant national activities and of environmental health data available, and of those factors that may be important in interpreting the data.

It is envisaged that international information synthesis will be provided for

a. Trends and levels of air quality in urban areas

b. Selected parameters of water quality in some international river and coastal waters

c. Selected parameters of food quality

d. Epidemiological studies on environmental health effects

e. Changes in mortality and morbidity data that may be related to environmental influences, and of other selected environmental health indicators.

3. Environmental monitoring

Although it is accepted that priorities may vary from one country to another, the selection of environmental factors to be monitored must be based on an agreed set of criteria. Considerations that need to be taken into account when establishing priorities are the same as for the pollutants mentioned earlier.

It has to be recognized that some of the prioritized agents will not satisfy all of the criteria in every country. It is apparent that while many would be of particular importance to the developed countries, the problems of developing countries may differ. Therefore, it may not prove practicable to include all of the measurable priority environmental agents in the initial phase of the international environmental health monitoring program.

Elements of the program are

1. Comparability of measurements and data quality control
2. Design and operation of monitoring networks
3. Data acquisition and analysis
4. Emergency response teams
5. Training and fellowship programs and
6. Research and Development through international coordination.

Specific program areas would address

1. Air Quality

2. Water Quality
    a. Inland water bodies
    b. Coastal waters
    c. Drinking water supplies

3. Food Contamination

4. Occupational and Home Exposures

5. Integrated Monitoring Systems

6. Environmental Radiation and Other Physical Factors

7. Monitoring of Health Effects
    a. Routine data
    b. Health indicators
    c. Special surveys

Health Early-Warning System

The establishment of a health surveillance system which would provide an early-warning of adverse environmental effects is an extremely difficult program area and should be considered as a part of a much wider program on early warning systems of significant changes in the health status of the community.

An adequate warning system in WHO's opinion must be characterized by four mutually supporting program activities: first, epidemiologic studies to detect the first significant changes in the frequency or tempro-spatial distribution of selected health events; second, an integrated environmental monitoring system that can signal environmental changes perhaps several decades before the health effects become manifest; third, development of generalized and specific human exposure models so that range estimates of human exposures can quickly link environmental monitoring data to primary and secondary health data sources for effects studies; and fourth, the ability to activate appropriate toxicologic and clinical testing systems which can determine the biological plausibility and coherence of the suspected adverse effects. The components of the above system could also be used to document the beneficial health effects of different environmental control strategies.

A COST-RISK-BENEFIT ANALYSIS OF TOXIC SUBSTANCES

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ABSTRACT

Hundreds of new toxic substances are produced each year to satisfy consumer demand, but many of them also enter the environment as risks to the exposed population and to ecosystems. The most logical criterion for their control is a net comparison of all product gains and risk losses from using these substances, with the objective of maximizing the overall welfare of society. The operational framework presented here attempts to synthesize cost-benefit and risk information into a decision-making setting for the purpose of identifying the optimal control level. Both quantitative and qualitative value systems are merged into a single framework, and sequential stages of the analysis are outlined in detail. Several decision-making approaches are recommended, the appropriate choice depending upon the extent of risk-benefit data available as well as the preference for monetary versus nonmonetary values. Uncertainty in the data base complicates the assessment since its inclusion requires the application of special statistical measuresof confidence.

INTRODUCTION

As a result of rapid technological changes and industrial development, a large and increasing number of toxic and hazardous substances enters the environment or appears in consumer products each year. Because so many of these elements are generated without stringent regulations, or perhaps with no controls at all, man and nature have been involuntarily exposed to their effects. Some toxic substances cause known potential hazards to human health or ecological habitats, but the majority is not well understood and thus introduces uncertain risks to the environment.

In view of these informational deficiencies, policymakers face the complex task of setting optimal standards on product content and environmental quality. This problem becomes particularly acute with early warning systems, designed to recognize potential dangers from harmful chemicals and organisms. The limited time horizon for early warning precludes an extensive, detailed analysis of risks and benefits. Yet regulation, to be effective over the long run, cannot rest simply on intuitive decisions or arbitrary preferences. Inherent values and needs of society must be identified and, if possible, quantified in a framework that reveals the major welfare impacts of regulation. There is consequently a need for the development of methods to assess the cost-risk-benefit trade-offs of alternative decisions.

In the National Academy of Engineering's colloquium on benefit-risk perspectives, Lind(1) emphasized the importance of quantitative approaches. He was "disturbed by the absence of an understanding of the basis principles and methodology of decision analysis and benefit-cost analysis...". He further stated, "Some people will contend that it is impossible to quantify the outcomes of many social programs. To this I would answer that without quantification of the most basic nature it is impossible to specify a rational criterion for the evaluation of any program".

Echoing this observation, the President's Science Advisory Committee(2) argued that the absence of quantitative information is likely to bias regulations toward the overprotection of health and ecology. While risk avoidance is a necessary consideration, its value to society should be contrasted with that of products generating or containing toxic elements. The cost of incomplete information could have serious outcomes, as the Committee recognized: "Regulatory decisions in the name of protection of health and environmental integrity often have expensive consequences. They typically obligate large expenditures of money, they are meant to remain in effect over long periods of time, and they typically rearrange large areas of our lives. Given the large impact of these consequences, the decisions producing them deserve the best foundation possible. Errors in regulatory judgments can be extraordinarily expensive, in human and monetary terms."

This study presents a conceptual framework for a cost-risk-benefit analysis, hereafter called a CRB analysis. Operational stages of analysis are identified as they contribute to the optimal decision of maximizing social welfare. The utilitarian value of the method is limited by inadequacy of data, particularly on the risks from toxic substances. However, a methodological framework is important even prior to application. By outlining data requirements, it results in the selective processing of information. Otherwise, the decision-maker could become enmeshed in an unmanageable, largely valueless data bank.

Traditional cost-benefit analysis translates all impacts into economic magnitudes. Obviously, the use of a common denominator, such as the current dollar value, simplifies the task of selecting that control level at which toxic substances yield the highest net benefits to society. Unfortunately, many risks and benefits cannot be easily quantified in economic terms.

Muellhause(3), for example, claims that risks cannot be valued simply as the product of their cost times the probability of their occurrence. There is also a "nonpecuniary type of boundary condition", which governs the behavior of populations at risk. A much broader concept than that of the traditional analysis is thus recommended. The framework presented here can apply to either conceptual approach - the pure economic or the more comprehensive analysis.

CONCEPTUAL FRAMEWORK

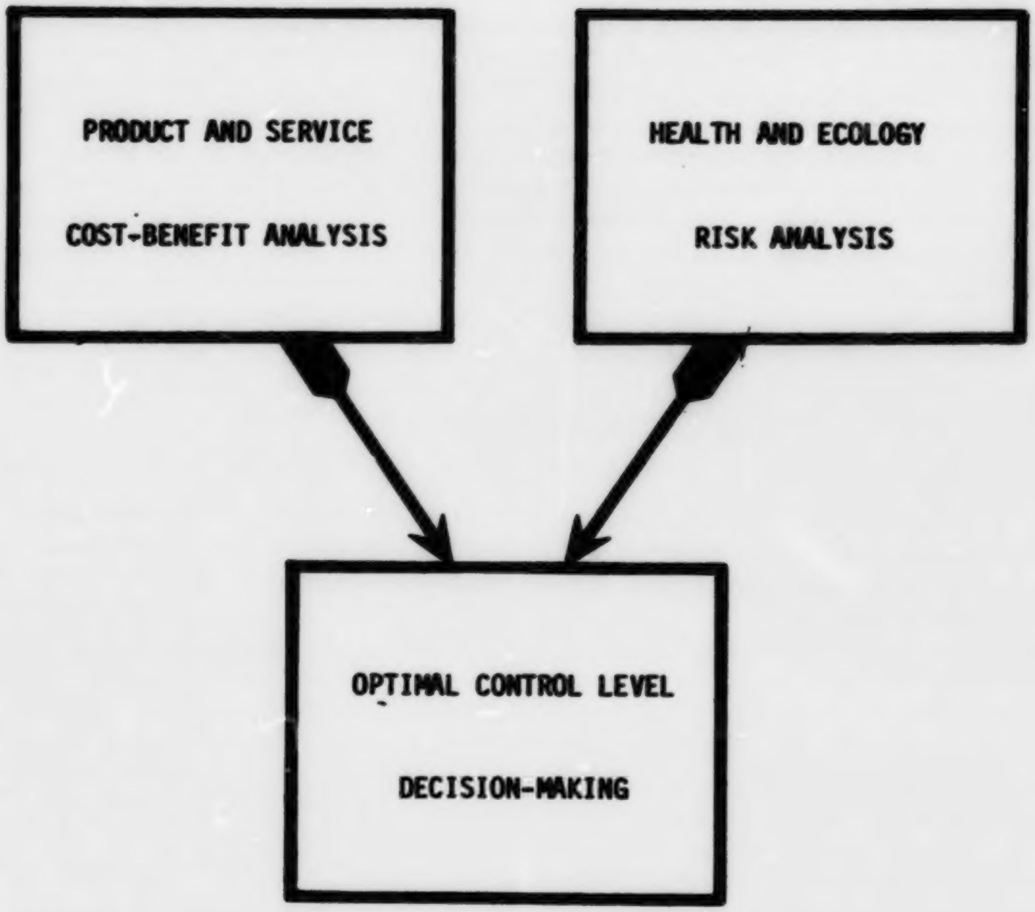
The term, cost-risk-benefit analysis, implies that decisions on toxic substances are based on some sort of accounting scheme of desirable versus undesirable outcomes. Almost every decision involves elements of risk in addition to benefits, and their assessment is often subjective and based on uncertainties. At the national level, an error of judgment can have serious repercussions, in the future if not at present. The outcome can affect a large segment of society and can disrupt or perturb economic growth. Notably in the protection of health and safety, the public is demanding more than ever that strong legislation be enacted to enhance the overall welfare of society. With hundreds of new toxic chemicals manufactured each year, this demand becomes more challenging. As a result, legislators are confronted with the difficult evaluation of risks and damages (both immediate and probable) and balancing them against social benefits of using toxic substances.

Risk-benefit assessments have evolved into a comprehensive, systems framework in order to compare a variety of welfare trade-offs.(4) To develop and utilize this framework requires multidisciplinary expertise. Economists have contributed methods and theory for the measurement of social welfare impacts based on market prices or personal willingness-to-pay.(5) Statisticians have derived confidence intervals and other probabilistic measures to assess the degree of risk or benefit uncertainty.(6,7) Ecologists and health experts have conducted various experiments and research to test animal (and less frequently human) responses to specific toxic materials.(2,8) But most of these tests have been confined to acute, rather than low-level or long-run, exposures. To utilize this information on risks and benefits, operations research analysts have devised methods of determining socially optimal decisions for toxic and other substances. Some of these techniques are designed especially to handle risk uncertainty, e.g., see Reference (9).

Figure 1 abstracts the operational framework for an evaluation of environmental quality. Although the analysis pertains to the control of toxic substances, it can be generalized to other objectives, such as the assessment of competing energy sources. Both economic and non-economic factors are represented. Product and service benefits can usually be measured in monetary units. But many social and ecological risks defy quantification and currently are not well understood. To neglect the latter effects in a CRB analysis would yield a partial, and probably misleading, solution of welfare optimization.

According to this diagram, the analysis of toxic substance controls is delineated into three components. First, the cost-benefit assessment pertains to net economic losses attributable to changing consumer demand and supply for products or services subject to controls. Costs can include the treatment of toxic effluents, the substitution of nontoxic for toxic products, and process modifications to alter toxic input requirements or product composition. Benefits respond to each person's willingness-to-pay for the consumption or use of items containing toxic substances or generating them as waste residuals. Net benefit losses can be expected when productive resources are shifted from manufacturing or service sectors into toxicity control programs.

Less amenable to monetary evaluation are risks to human health and ecological systems. The risk analysis attempts to translate these probabilistic states, wherever possible, into expected damages or welfare losses. For some risk categories, quantification is currently infeasible. By controlling toxic substances, risks are avoided, thereby



PRODUCT AND SERVICE
COST-BENEFIT ANALYSIS
HEALTH AND ECOLOGY
RISK ANALYSIS
OPTIMAL CONTROL LEVEL
DECISION-MAKING

FIGURE 1. BROAD CONCEPTUAL FRAMEWORK FOR IMPACT ANALYSIS OF TOXIC SUBSTANCE CONTROLS

enhancing the safety and welfare of society and preserving environmental amenities.

Both the cost-benefit and risk analyses provide input data for the decision-making component. Here, economic and ecological consequences of various toxicity control levels are compared, and the best solution is found via one of several optimization techniques. The choice of a technique to identify this level is influenced by the type and extent of available benefit-risk information. In the case of early warning systems, only a shortened version of the complete CRB evaluation is feasible because of time constraints on the collection and analysis of data.

COST-BENEFIT ANALYSIS

The operational elements of a cost-benefit analysis are outlined in Figure 2. Arrows in the diagram portray the flow of information among sequential steps. The first step entails the preselection of all benefit categories, α_1, $\alpha_2, \ldots$, which depend on the direct or indirect utilization and consumption of toxic substances. An example is the demand for pulp and paper, whose production generates mercury-containing residuals. Effluent controls on these residuals could be so stringent as to aggravate price hikes. Increased costs of control are thus eventually passed on to the consumer, who disbenefits either by paying more per unit of product or by discontinuing his purchase.

For increasing control levels, C_1, $C_2, \ldots$, as defined in Step 2, prices respond in corresponding fashion. Step 3 depicts a typical consumer response, also illustrated in more detail in Figure 3. At control level C_1, the price of product (or service) α_1 is $P_{1\alpha}$; while at C_2 it becomes $P_{2\alpha}$.

A price hike ordinarily implies welfare losses to the consumer of that product. This impact is derived in Step 4 (of Figure 2). As shown more fully in Figure 4, the equilibrium price moves up the demand curve with increasing controls. From welfare economic theory, total benefits are measured as the area under this curve but above the price line. That is, benefits to each consumer equal the difference between the actual price and what he is willing to pay. Some individuals will pay as much as U, while marginal consumers will pay no more than the current price $P_{1\alpha}$. If the unit price increases to $P_{2\alpha}$, the marginal consumer (at $P_{1\alpha}$) is no longer willing to buy the product or service. Benefit losses from decreased demand

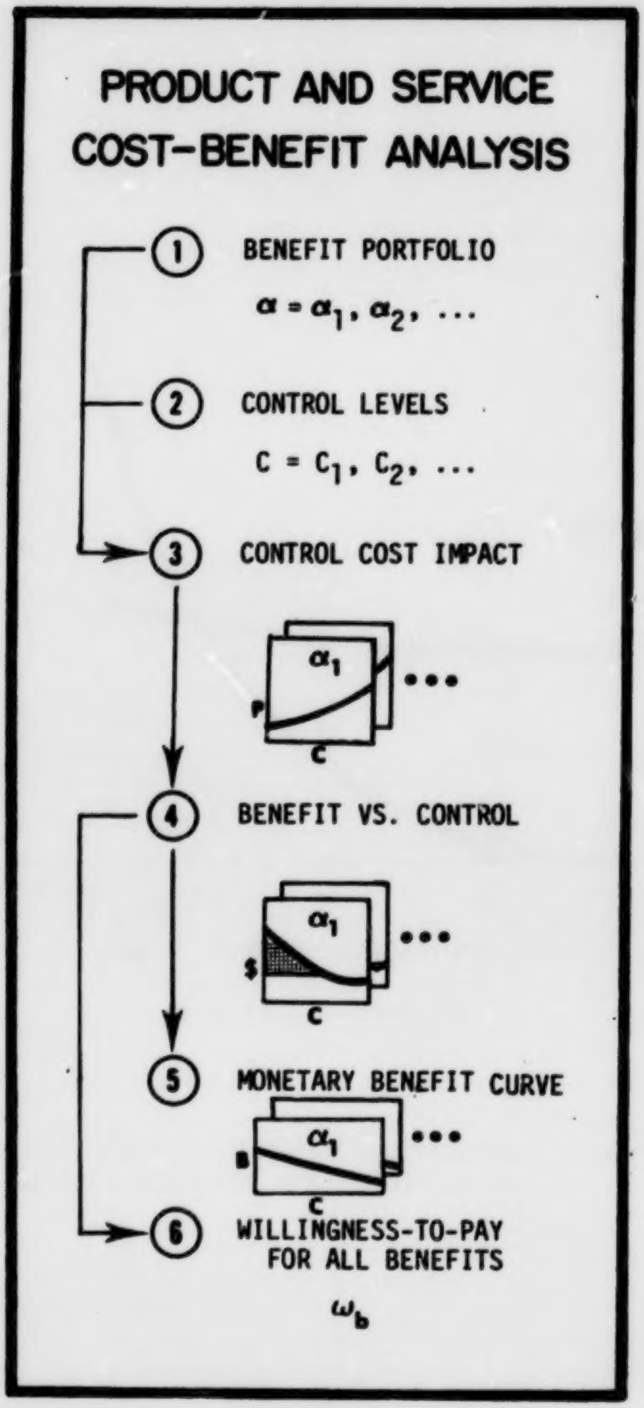

PRODUCT AND SERVICE
COST-BENEFIT ANALYSIS
① BENEFIT PORTFOLIO
$\alpha = \alpha_1, \alpha_2, \dots$
② CONTROL LEVELS
$C = C_1, C_2, \dots$
③ CONTROL COST IMPACT
α_1
P
C
④ BENEFIT VS. CONTROL
α_1
\$
C
⑤ MONETARY BENEFIT CURVE
α_1
B
C
⑥ WILLINGNESS-TO-PAY
FOR ALL BENEFITS
ω_b

FIGURE 2. SEQUENTIAL STAGES OF COST-BENEFIT ANALYSIS

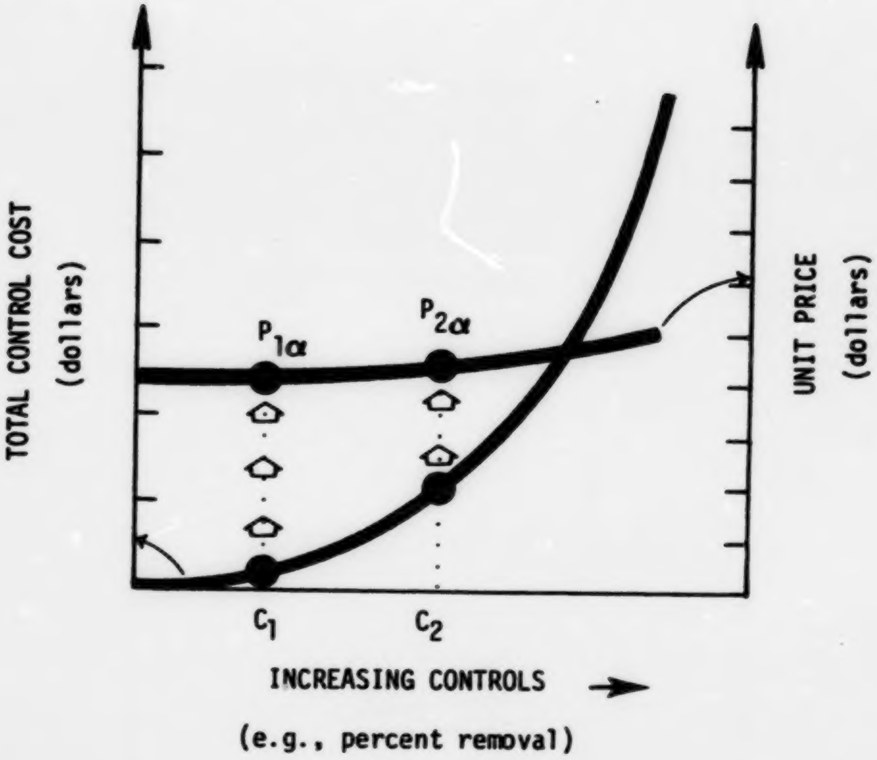


FIGURE 3. IMPACT OF VARIOUS CONTROL LEVELS ON PRODUCT OR SERVICE PRICES

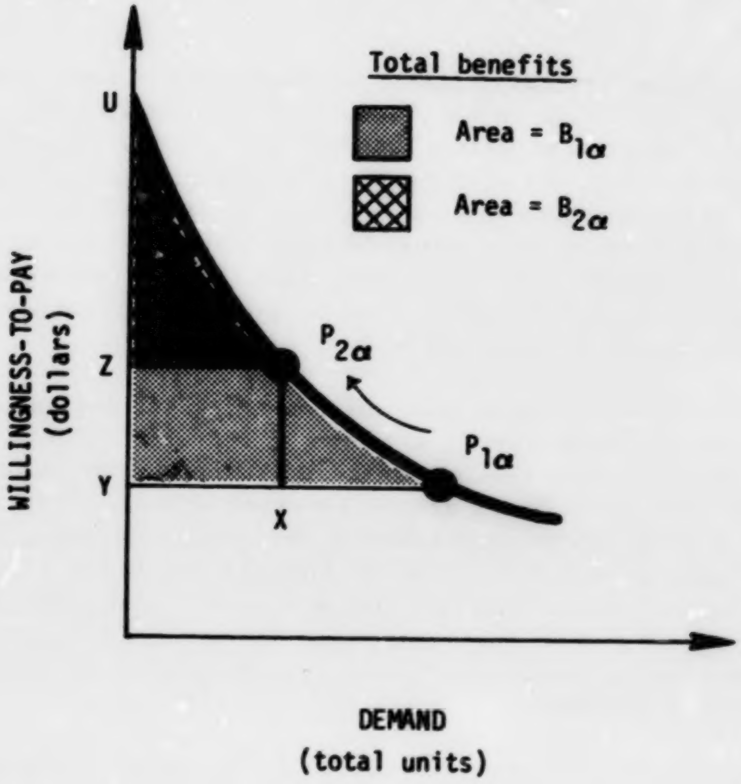


FIGURE 4. ESTIMATION OF PRODUCT OR SERVICE BENEFITS FOR VARIOUS CONTROL LEVELS

are then estimated by the area, $XP_{1\alpha}P_{2\alpha}$. Additional disbenefits are incurred by the remaining consumers, who pay an additional $P_{1\alpha} - P_{2\alpha}$ per unit. Welfare losses for these individuals equal the rectangular area, $XYZP_{2\alpha}$. Total disbenefits to society are thus estimated as $XYZP_{2\alpha}P_{1\alpha}$.

These losses are based not on the direct use of toxic substances, but rather on their effect on the price of directly consumable items. Provenzano(10) argued similarly that the value-in-use of such inputs can be measured in terms of the generated output. But he also contended that in cases where this value cannot be isolated for the input in question, benefits must be measured by an alternative method. If the producer must substitute another input, then the appropriate estimate is the additional cost of doing so, also called "the opportunity cost of not being able to use the original input".

Step 5 of Figure 2 translates the consumer surplus estimates (Figure 4) into a benefit curve, as shown in Figure 5. There are numerous sources of uncertainty in these estimates, which account for the wide confidence bands around expected values. For example, only a subset of the entire population is sampled in deriving demand curves. Biases in willingness-to-pay surveys are another source of error. If the respondent believes that his answer will affect prices, he may purposely give a lower estimate. Or perhaps he is unsure of the value and thus gives different answers, depending on the time at which he is interviewed.

It must be noted that benefit losses for product α_1 represent only one impact of consumer demand. If there is a close substitute for this item, then its benefit losses will be partially negated by increased consumption and hence greater benefits for the alternate product or service. To account for net benefit changes thus requires the identification of all significant impacts, whether they are direct or indirect, competing or complementary, short-term or (discounted) long-term. Added together, the individual product and service benefits provide an estimate of total social impacts.

An alternate method of estimating net benefits is to derive a willingness-to-pay curve (Step 6) representing all impact simultaneously. By means of survey techniques, individuals are asked to estimate the amount that would represent sufficient compensation (excluding risks) for reducing current use of toxic substances. Their answers are then plotted against various toxicity control levels, and a benefit curve ω_b is then fitted through these sample observations.

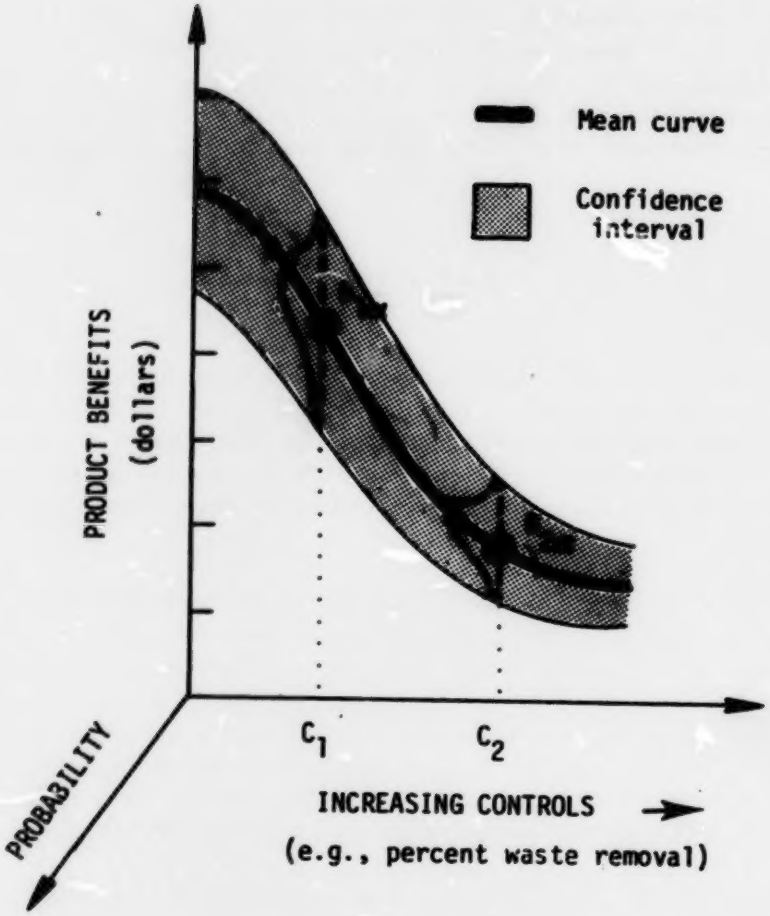


FIGURE 5. FORMULATION OF PRODUCT OR SERVICE BENEFIT CURVE

Theoretically, this curve should be equivalent to the net sum of all single product and service benefit curves derived in Step 5. But this assumes that each individual is perfectly knowledgeable about the totality of benefits. In practice, willingness-to-pay values are more likely to reflect a narrow, self- rather than society-oriented perspective. Biases in these values can thus be anticipated. For instance, an individual will be conservative if he fears that his answer might affect his tax base, while an overestimate is probable if he suspects that other members of society will be responsible for payment.

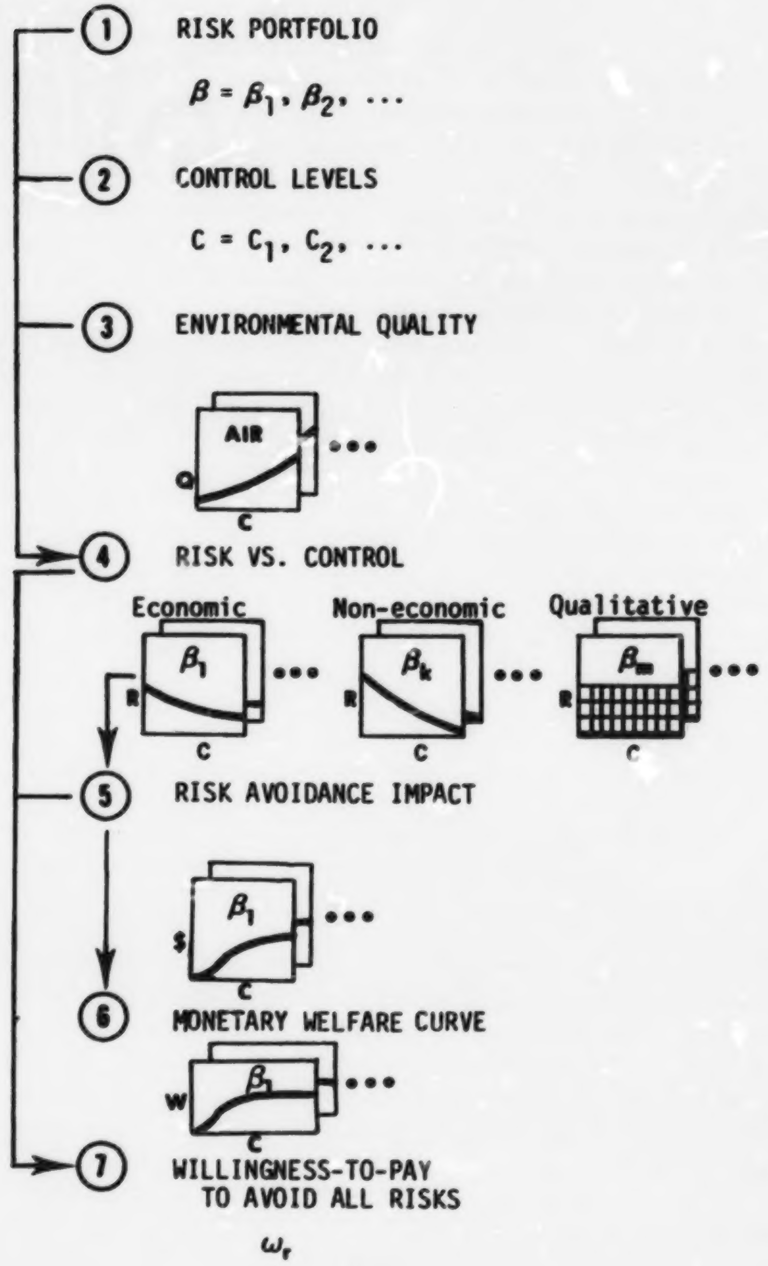
RISK ANALYSIS

Risks to human health and ecological systems constitute the second component of the conceptual framework. As toxic substances are removed from the environment or the food chain, risks should decline correspondingly. Social benefits from such action include an improvement in the health, safety, and general welfare of the exposed population.

The assessment of these impacts is described in Figure 6. Step 1 enumerates specific categories of either known or suspected risks. If control levels (Step 2) refer to emission loads, they must be transformed into ambient concentrations of toxic substances to which the population at risk is exposed. Step 3 shows a typical model, whereby effluent loads are translated into ambient conditions by a waste diffusion process. Other examples may be more complicated to predict, such as the accumulation of mercury derivatives in fish.

Risk levels are then related to environmental quality according to Step 4. This step is very crucial to the analysis, as it involves the assessment of risks, either probabilistic or deterministic, over a range of quality (or control) levels. Three types of risk are differentiated. Some risks can be monetized, e.g., medical costs and lost wages from illness. Other can be also quantified, such as pollution tolerance levels of fish species, but their translation into economic values is questionable. Either the item at risk has no price in the marketplace, e.g., seagulls, or else it indirectly supports commercial products but is not demanded in itself, e.g., phytoplankton in the food chain culminating with commercial fish. Still other risks currently defy any numerical or physical quantification, but are described in qualitative fashion. The preservation of environmental intangibles such as aesthetics falls within this domain.

HEALTH AND ECOLOGY RISK ANALYSIS



① RISK PORTFOLIO
β = β1, β2, ...
② CONTROL LEVELS
C = C1, C2, ...
③ ENVIRONMENTAL QUALITY
AIR
Q
C
④ RISK VS. CONTROL
Economic
Non-economic
Qualitative
β1
βk
βm
R
C
⑤ RISK AVOIDANCE IMPACT
β1
$
C
⑥ MONETARY WELFARE CURVE
β1
W
C
⑦ WILLINGNESS-TO-PAY TO AVOID ALL RISKS
ωr

FIGURE 6. SEQUENTIAL STAGES OF RISK ANALYSIS

Because risks are probabilistic and must usually be assessed without adequate data, their mean values serve limited objectives. Instead, a stochastic interpretation of each risk level is more relevant. According to Figure 7, this interval is bounded along the lower border but not along the upper one. This distinction occurs for at least two reasons. First, in addition to typically mild cases of exposures, there may be isolated reports of serious episodes, e.g., human fatalities, caused by extended exposure to toxic substances. These observations could fall far above the typical or mean risk curve. Second, but more importantly, there are unknown or as yet undiscovered risks whose recognition would either shift the mean curve upward or extend the confidence range far above the mean. Because early warning systems must weigh such uncertainties, the confidence band should reflect the likelihood of future problems. Thus, unlike the balanced Gaussian distribution underlying most confidence measures, this band would be skewed toward high risk values. Note that this function ranges over the original control level, which is derived from ambient quality according to the diffusion model in Step 3.

The next step results in the transformation of risk avoidance into an expected economic return. As the risk of human accidents, sickness, or fatalities decline, savings can be anticipated in terms of lower medical costs, higher wages from reduced absenteeism at work, etc. An expected value of these savings is depicted by the upward sloping curve.

Finally, to circumvent the task of developing individual risk curves, willingness-to-pay surveys can be conducted to derive an aggregate welfare index. Analogous to that derived in the cost-benefit analysis, the function ω_r (Step 7) depicts total economic gains of reducing all risks simultaneously, as controls on toxic substances become more stringent.

In Figure 8, a typical welfare function is derived from increasing risk avoidance levels. An S-shaped form is illustrated, with a horizontal asymptote defining maximal expected welfare. This limit is necessary since each individual, with a finite income, can afford only a limited insurance premium to protect his health from unknown events. The S-shape has been empirically justified in a survey(11) of the amount, ω, that people are willing to pay to reduce their probability, ρ, of heart attacks and premature death. Mathematically, this function is written as,

$$\omega = e^{a+b/\rho} ,$$

where a and b are regression coefficients. Typical confidence bands

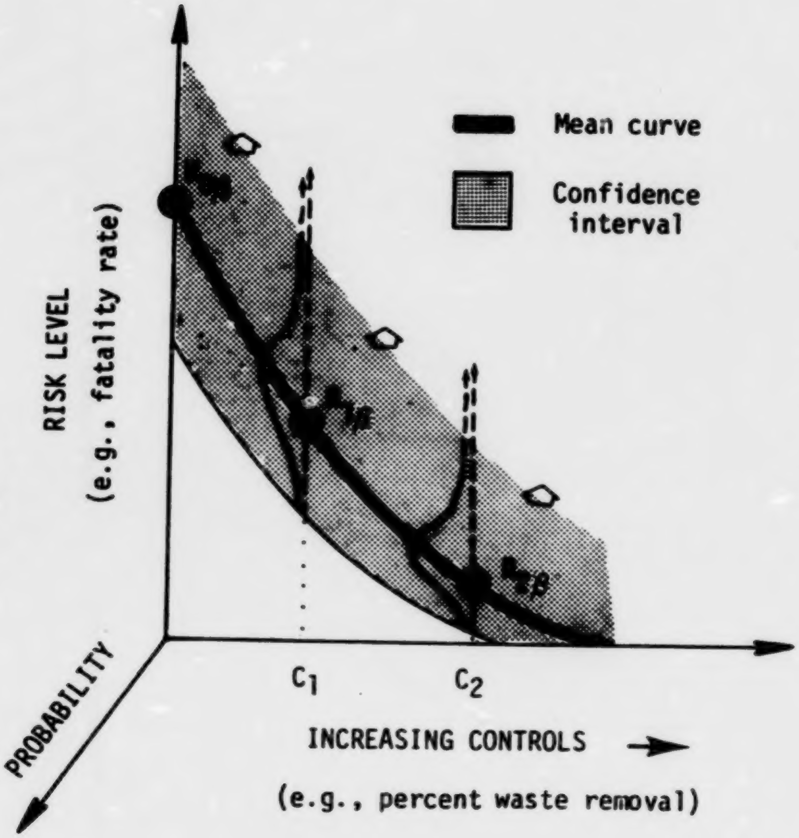


FIGURE 7. ESTIMATION OF RISKS AT VARIOUS CONTROL LEVELS

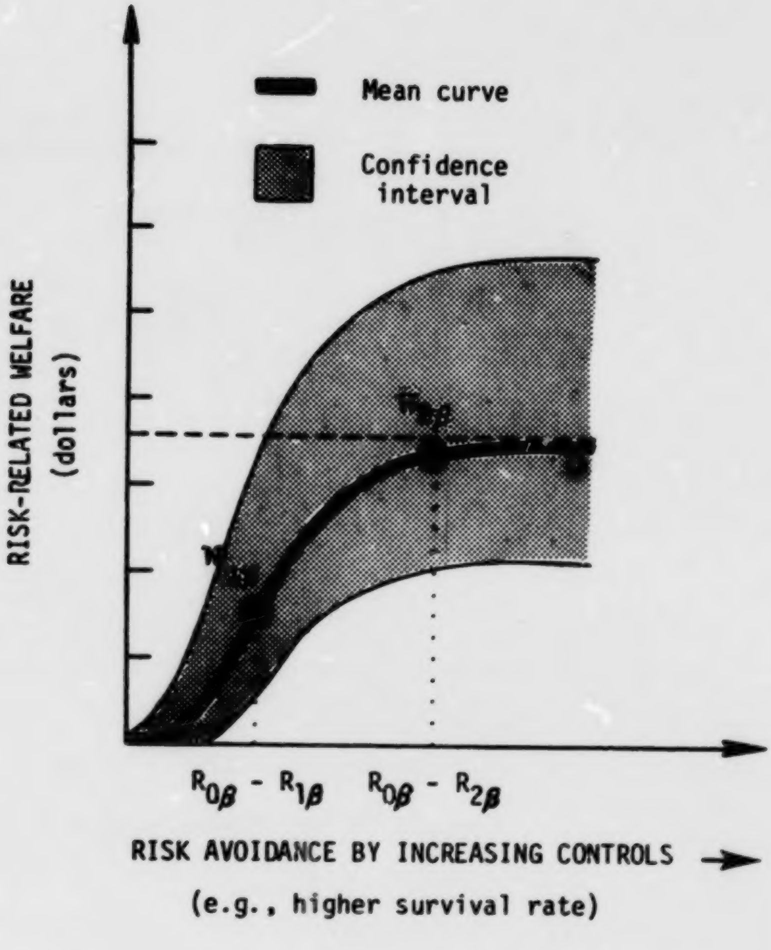


FIGURE 8. ESTIMATION OF RISK-REDUCTION-WELFARE IMPACTS AT VARIOUS CONTROL LEVELS

for this regression show the variation of people's perception of welfare. The distribution of family incomes influences this variation, with wealthier respondents generally willing (and able) to contribute more dollars.(12)

In addition to purely monetary values, there has recently been concern about the "nonpecuniary demand for safety".(3) Irrespective of monetary welfare impacts, this consideration could lead a consumer to reject a toxic substance-bearing product for a number of personal reasons, including the following: "...his talent and ability to manage the operation of the product in question, his past experience and success of similar undertakings, and his natural propensity or aversion for assuming risks". To compensate for this nonpecuniary impact, the welfare curve is multiplied over its entire risk avoidance range by a factor exceeding unity. Although this factor has been described in theory, it has never been measured empirically, and therefore remains subject to debate.

DECISION ANALYSIS

After risks and cost-benefit impacts are evaluated, the decision-maker can compare them for the purpose of setting optimal control levels. The objective is to set standards so as to maximize social welfare, mathematically stated as the present discounted value of all product and service benefits plus total risk avoidance gains. Figure 9 depicts four alternate approaches to optimization. The selection of an approach depends not only on the extent of information but on the extent of monetary data. The economic analysis, which relies completely on dollar values, can proceed as a complete or partial assessment. The former relates total willingness-to-pay to changing levels of toxic substance use. By superimposing the benefit and risk avoidance functions, ω_b and ω_r, respectively, a social welfare curve is derived as their sum. Figure 10 illustrates the manner in which the best decision is identified. From differential calculus, the social optimum C_* is that point at which the derivative of the social welfare curve vanishes. (In cases where there are several local optima, the decision-maker must choose the best solution.)

The optimal solution is not so obvious as this simplified graph indicates. Willingness-to-pay curves for each benefit or risk (see Figures 5 and 8) reveal that uncertainties play a fundamental role in the analysis. Consequently, the social welfare function becomes a

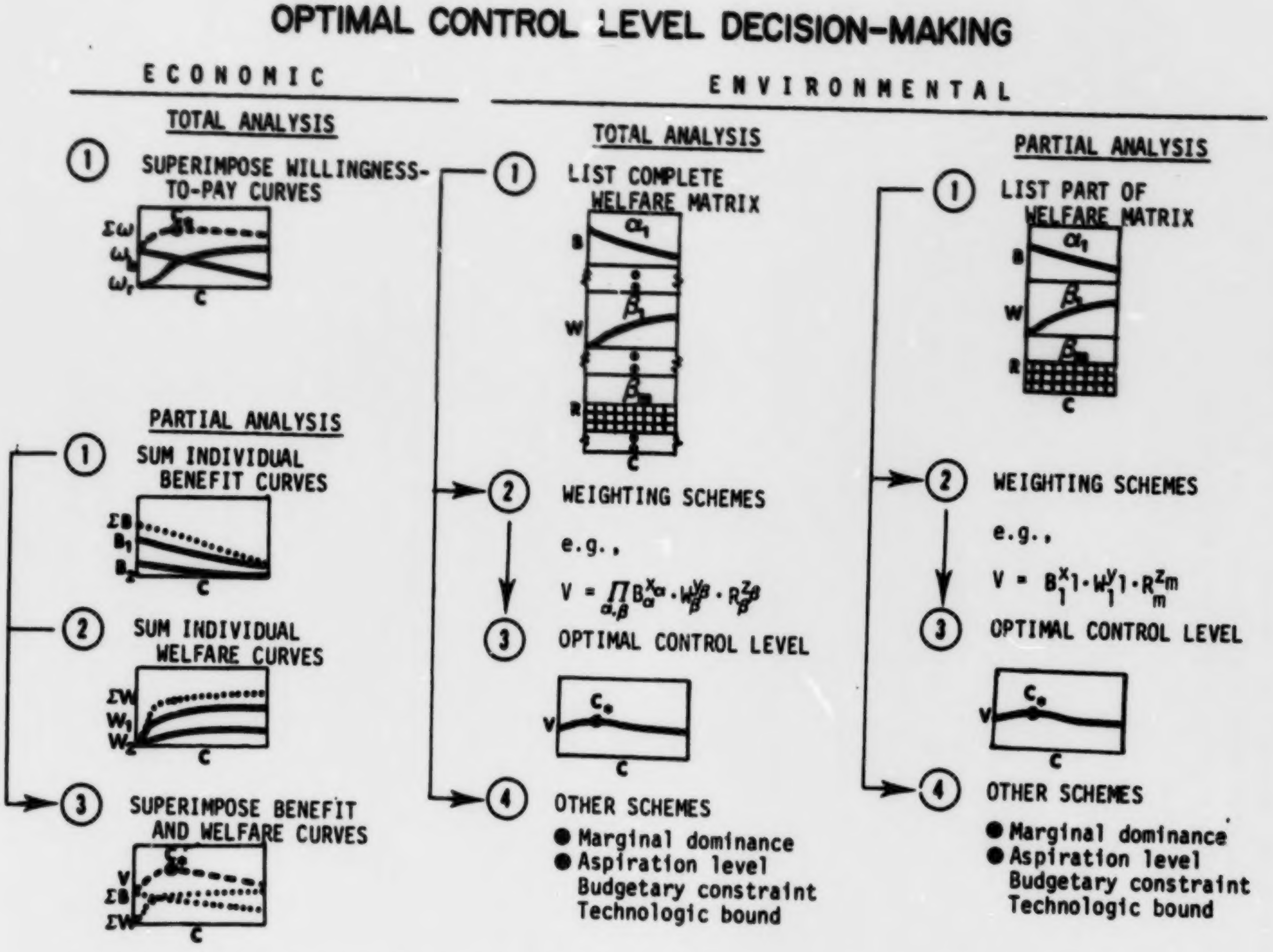

OPTIMAL CONTROL LEVEL DECISION-MAKING
ECONOMIC
TOTAL ANALYSIS
① SUPERIMPOSE WILLINGNESS-TO-PAY CURVES
Σω
C_0
ω_1
ω_r
C
PARTIAL ANALYSIS
① SUM INDIVIDUAL BENEFIT CURVES
ΣB
B_1
B_2
C
② SUM INDIVIDUAL WELFARE CURVES
ΣW
W_1
W_2
C
③ SUPERIMPOSE BENEFIT AND WELFARE CURVES
V
ΣB
ΣW
C_0
C
ENVIRONMENTAL
TOTAL ANALYSIS
① LIST COMPLETE WELFARE MATRIX
B
W
R
α_1
β_1
β_m
C
② WEIGHTING SCHEMES
e.g.,
$V = \prod_{\alpha,\beta} B_\alpha^{x_\alpha} \cdot W_\beta^{y_\beta} \cdot R_\beta^{z_\beta}$
③ OPTIMAL CONTROL LEVEL
V
C_0
C
④ OTHER SCHEMES
● Marginal dominance
● Aspiration level
Budgetary constraint
Technologic bound
PARTIAL ANALYSIS
① LIST PART OF WELFARE MATRIX
B
W
R
α_1
β_1
β_m
C
② WEIGHTING SCHEMES
e.g.,
$V = B_1^{x}1 \cdot W_1^{y}1 \cdot R_m^{z}m$
③ OPTIMAL CONTROL LEVEL
V
C_0
C
④ OTHER SCHEMES
● Marginal dominance
● Aspiration level
Budgetary constraint
Technologic bound

FIGURE 9. SEQUENTIAL STAGES OF OPTIMAL DECISION-MAKING STRATEGIES

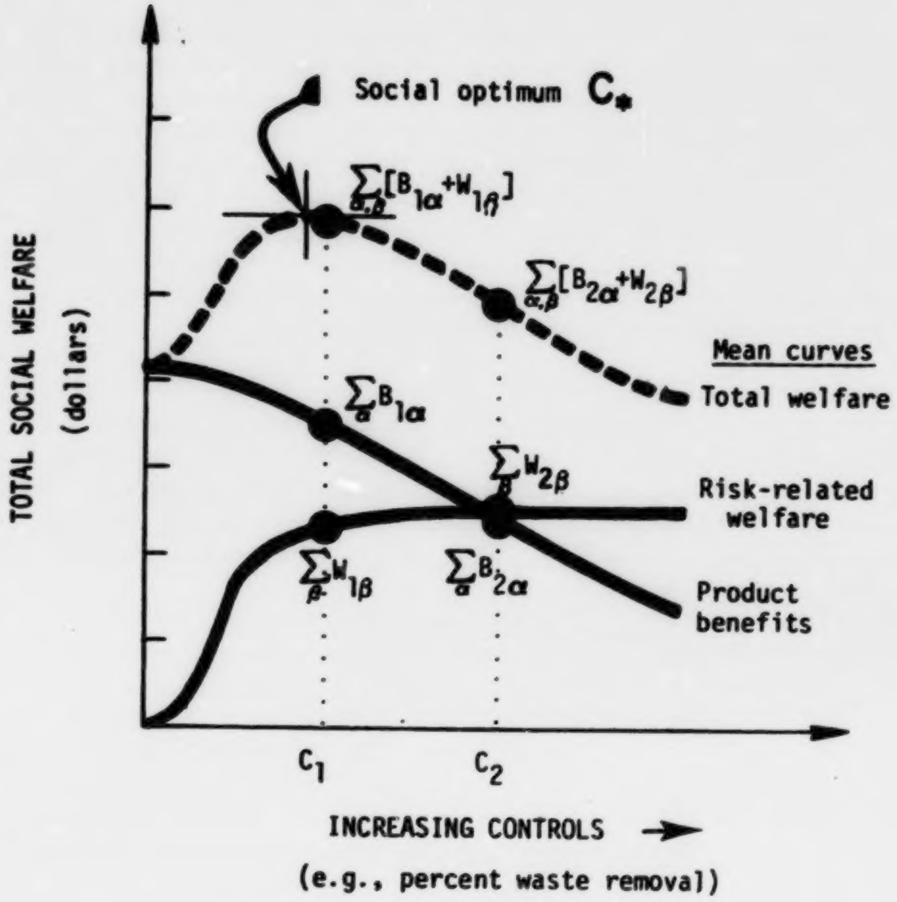


FIGURE 10. SELECTION OF OPTIMAL CONTROL LEVEL IN RISK-BENEFIT ANALYSIS OF TOXIC SUBSTANCES

confidence band surrounding the mean curve. The optimum is translated into an interval of likely values with a derived probability distribution, rather than a single value. The decision-maker is most likely to select themean value or a higher one, if he is risk averse.(13)

To be meaningful, willingness-to-pay curves should reflect the totality of benefit impacts. However, no individual has a clear perception and understanding of all market and economic factors. Moreover, there are inequity issues underlying one's ability to pay. Family income levels will affect the magnitude of his response. In at least one empirical study(12), willingness-to-pay was found to increase significantly with rising incomes. At very high incomes (exceeding $50,000) this trend tapers off and even dips slightly. Because of such distributional questions, willingness-to-pay values are not widely accepted in measuring economic impacts.

Another approach based solely on monetary trade-offs is a partial assessment. Several important benefit and risk avoidance functions are summed together to derive a social welfare function, after which the optimal control point (or interval) is determined. Provided that the economically most significant curves are chosen, this partial approach should provide a reasonable approximation to the actual (total impact) solution.

The above optimization strategies rely on monetary values. Obviously, there are nonquantifiable aspects of the environment as well. The remaining strategies in Figure 9 are called "comprehensive" since they include noneconomic and economic data. In the complete analysis, all risk and benefit portfolios are enumerated (Step 1). To permit comparability of these values for policy-making purposes, all risk-benefit impacts must be determined over the same range of control levels.

This one-to-one correspondence makes it possible to compare marginal impacts by sight, and thus to quickly identify those control levels likely to yield the greatest overall changes in risks and benefits. The next three steps describe methods of selecting the best policy. First, a weighting scheme can be applied, such that magnitudes of risks and benefits are substituted into a "value function". This function can be exponential (as shown) or some other form, whose value V rises as individual benefits increase or risks decline. Values are thus calculated over all control options, and a maximal level C_* is found (Step 3).

Although weighting functions have been used in actual studies [e.g., see Reference (14)], they lack general popularity. Since relative weights must be assigned, such functions explicitly trade off monetary and nonmonetary impacts. Of course, any decision-maker is ultimately faced with this problem in designing policy; but to explicitly interrelate such impacts raises objections among ecologists, many of whom claim that environmental quality cannot be described in dollar terms. Another objection is that all dependent variables in the weighting fuction must assume numerical values, thus conflicting with the meaning of nonquantitative risks.

The simplest, and perhaps most popular, solution is to promote "zero tolerance" of toxic elements. That is, their use is completely banned, in an effort to minimize health risks. From a social welfare point of view, this approach is probably inefficient since it fails to consider the benefits side.

Of greater appear to environmentalists and economists alike is a quasi-optimization approach called "marginal dominance". The decision-maker inspects risks and benefit curves individually, and identifies those control levels at which marginal (changing) impacts are extreme. From previous remarks on willingness-to-pay, these marginal conditions may indicate the optimal solution. But when there is a large number of such impacts, numerous control levels will be identified. Consequently, the problem then reduces to choosing one optimum. This choice depends on the implicit ranking of marginal risks and benefits by the decision maker. Thus, a value system must still be applied, but at least it is not so obvious as to be repugnant to many environmentalists.

CONCLUSION

Policies on toxic substance control should not be derived from subjective opinion. If welfare of society is to be optimally enhanced, a quantitative analysis of benefits and risks is the most promising approach. Recently, in fact, scientists have strongly advocated the development of methods to assess competing impacts of product benefits versus risks from exposure to toxic elements.

An operational framework is presented here for the purpose of assessing welfare impacts of product or service benefits, health or ecological risks, and then utilizing them in a decision-making analysis. There are several approaches to selecting the optimal control level, each appealing to a distinct audience and having specific advantages. Economic approaches are simplistic in that they assume only monetary values. Willingness-to-pay surveys provide a quick method of assessing the total value of risks and benefits, but their plausibility is frequently questioned. Individual risks and benefits can be listed in a partial assessment, but the adequacy of this list may be difficult to ascertain. Moreover, a large number of these categories may be necessary to cover a substantial portion of total effects.

To the noneconomist, complete dependence on monetary values is frequently unacceptable. There are intangible or noneconomic aspects of the environment that should also be assessed. To comply with their value system, a more comprehensive approach is developed. Here, as with the pure economics approach, the amount of risk-benefit data available determines whether a total or partial assessment is appropriate. The latter is more likely in view of the limited time horizon over which controls on toxic substances must be established.

Because risks and benefits are not necessarily translated into the same units, e.g., dollars, the optimization procedure is not straightforward. A weighting function can be derived by assigning relative values to impacts at various control levels, but this technique implies a direct comparison of monetary and nonmonetary impacts. An alternative method is to apply marginal dominance, whereby the greatest changes in specific risks and benefits are identified as controls become more stringent. These changes will indicate the most likely policies for welfare optimization.

On the risk side, there are several unresolved problems of assessment. One involves the role of uncertainty of the data base. A CRB analysis based on currently available information is likely to underestimate total impacts. As more knowledge about potential risks is discovered, the public seems more willing to pay to avoid these risks. An example is asbestos, which was of no concern fifty years ago but is now under intensive investigation because of recent findings on illnesses of asbestos plant workers.(15)

Another problem concerns the protection of any natural ecosystem or even a single species. While species fatality curves must be known, risks also pertain to changes in metabolic rates, reproduction rates, and modifications of the food chain. Complex linkages and survival dependencies within an ecosystem make this analysis particularly challenging. Moreover the accumulation and synergistic effects of toxic elements pose still another problem. To segregate the effects with respect to each element may be impossible.

The complexity of risk-benefit analyses is accented by the need to evaluate risks and benefits over the same range of control levels. This requires the translation of ambient exposure control levels (for risks) into control standards on emissions or product content. Provided that controls pertain uniformly to one industry or product, the analysis presented here is applicable. But if more than one generating source of toxic substances is involved, the control variable is multidimensional rather than single-valued (see Figure 3). In this case, the control parameter C is equivalent to a vector.

As shown here, the operational framework for a CRB analysis consists of numerous steps. In theory, however, the procedure can be explained more simply.(3) But the gap between conceptual models and their empirical application is surprisingly wide. The CRB analysis may be simplified to some extent by minimizing costs of controlling toxic substances, subject to the avoidance of certain risks. But this objective neglects the (often high) value of products containing or generating toxic elements. Instead, this study assumes that the control costs are eventually paid by the consumer in the form of higher prices, and hence that product benefit changes reflect these costs.

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The opinions expressed in this study are those of the authors and do not represent the official views of the Environmental Protection Agency.

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THE PROBLEMS WITH EARLY-WARNING SYSTEMS FOR TOXIC MATERIALS*

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ABSTRACT

The information required for the estimation of health and environmental impacts resulting from discharges and/or use of toxic materials is reviewed. An ideal system is proposed (the straw man approach) in which hazard is equated to the product of some function giving the exposure rate to man and other biota, and a function expressing the toxicity of a material. The information required to implement such a system including data on the flow of the material in society (manufacturing use, and disposal patterns), persistency and low level chronic exposure effects are enumerated. The difficulties in obtaining the information are discussed including cost and statutory limitations. Some alternatives to the ideal system are proposed.

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1974 - A YEAR OF TRANSITION

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INTRODUCTION

During the past several weeks, talk in Washington has centered in large measure on the achievements during 1973 – or perhaps we should say the events during 1973. All agree that it was a tumultuous year with our domestic and environmental concerns largely overshadowed by unprecedented political events at home and abroad.

1973 was to be the year when the momentum of the environmental movement began to take us around the corner in cleaning up the air and the water. Our arsenal of regulatory tools for insuring product safety and sound disposal practices was to be expanded. And a degree of harmonization was to be achieved between economic progress and environmental controls.

But this was not the case. Energy concerns threatened to reverse past environmental gains. Congressional attention was diverted from the details of environmental legislation. And perhaps most unfortunately the influx of top young talent into the environmental picture seemed to slacken.

However, environmental milestones were far from lacking during 1973. For example, in the area of toxic substances:

- The chemical industry is still reverberating from the Department of Labor's stringent interim standards for handling 14 carcinogens, including several of considerable commercial importance.

- FDA banned the use of DES as a feed additive over the strong objections of the cattle ranchers.

- EPA's promulgation of final air emission standards and proposed water effluent standards for toxic pollutants are causing major adjustments in manufacturing practices at many facilities.

- Promulgation of final leaded gasoline regulations culminated several years of effort to address the severity of the problem of lead inhalation and human health.

- Discovery of high levels of asbestos fibers in the Duluth water supply has catalyzed a large array of technical talent to address what could turn out to be either a sleeping giant or a false alarm of major dimensions.

- The tussock moth outbreak on the West Coast highlighted the environmental and economic "disbenefits" resulting from the ban on DDT.

- Finally, the National Center for Toxicological Research in Pine Bluff, Arkansas, became a viable operation that is making its mark in the regulatory world.

THE ISSUES FOR 1974

While the number and diversity of issues in the environmental field continue to grow, many of the most important questions to be addressed in the immediate future in my specific area of concern are the well-known "old chestnuts". Traditionally, we tend either to take these issues for granted or skirt them because of their difficulty. In either case we then focus on other questions which are also important but which could be irrelevant if our fundamental approach is not sound. Let me cite four of the "old chestnuts" which are certainly near the top of our list.

Toxicological Testing and Standard Setting: Can We Do Better?

Emblazoned in laws and in the Federal Register are standardized approaches to a very complicated science - standardized approaches that date back many years and, having gained a type of legal status, seem almost immune from scrutiny and revision. As an engineer I should feel comfortable in surrounding the biological sciences with accepted quantifiable approaches and easily defined safety factors, but

I am not. In my view, a thorough review – initially by the scientific community itself – of the currently accepted approaches to generation and interpretation of test data is needed.

In this regard, EPA recently proposed a numerical standard for the carcinogen benzidine based on the concept that in determining the standards, the level of risk which is acceptable must be considered in the light of the benefits derived from the chemical. Derivation of this level of risk requires types of test data not ordinarily generated by toxicologists, thus suggesting a significantly different approach to testing carcinogens, and perhaps other chemicals as well.

In large measure the issue revolves around how the scientist packages the toxicological data for the decision-maker. If the scientist structures the experiment and packages the data to derive simply a "safe" level for chemical exposure, then the decision-maker has only one option, and all other factors become irrelevant. The scientist has in fact assumed responsibility for consideration of the total impact of a regulation on society. On the other hand, if the scientist presents several options, with explanations of the health and environmental implications of each, then the decision-maker can indeed take into account a wide range of social and economic implications at different levels of chemical exposure.

Risk/Benefit Aspects of Toxic Substances: The Theorist or the Pragmatist?

Even though toxic substances are by definition dangerous to health or the environment, there seems to be general agreement that in developing control strategies some balancing of risks and benefits is in order, as reflected in the EPA action on benzidine. In the past, elaborate cost/benefit models have frequently had little operational relevance. At the same time we must do better than those past efforts that tend to focus only on the short-term, direct costs of environmental controls which are susceptible to quantification.

Perhaps the most formidable task is estimating the incremental gains to society – or the reduction of risks to society – by decreasing the level of a toxic substance entering the environment. Human poisoning, fish kills, and flora destruction can of course frequently be related to specific discharges. But these near-term, easily isolated incidents which can be used to correlate discharge levels with economic and social impact are the exception rather than the rule. A second problem is to estimate how much the level of exposure will be reduced by a specific control measure. Even if good monitoring data exist concerning current exposure levels, to project ahead the impact of a proposed measure is difficult indeed. And finally, of course, is the cost of the control measure, which usually involves much more than simply purchasing control devices. For example, in response to the Department of Labor restrictions on carcinogens, one company was forced to replace the carcinogen with another intermediate chemical which turned out to be far more cost/effective for the particular process. Had it not been for the regulation, and subsequent R and D effort by the company, this cost-saving innovation would still be lying dormant.

What should be the approach to risk/benefit analyses? With regard to the known problem substances, I suspect that in the short run we will do little better than weighted checklists to be used as general guidelines for at least surfacing some of the concerns before decision-making time. Case studies of specific past decisions should be particularly helpful in this regard. In the longer term, I don't know if a more objective approach can be developed that is broadly applicable to balancing risks and benefits.

However, a far more difficult problem faces us in answering the question: "How much is society ready to pay to search out other problem substances before they emerge as problems on the immediate horizon?" Or "What should be the cost of early warning?"

A Generalized Approach to Control Strategies for Multimedia Pollutants: Reality or Fantasy?

A number of the most troublesome toxic pollutants enter the environment from many sources, follow multiple routes through the environment, and come to rest in a variety of places. Studies have illustrated many of the complexities of movement and fate of pollutants. Such studies were particularly helpful in addressing the lead issue, as one example.

Can there be a generalized approach to control strategies for a large number of toxic pollutants with multimedia characteristics? Perhaps the behavioral and use idiosyncrasies of different chemicals require completely different approaches to the formulation of control strategies. Two of our most relevant experiences to date in developing control strategies have been the attempts to control selected toxic pollutants under different sections of the air and water legislation.

These single media approaches to control strategies clearly underscore the difficulty of generalized approaches.

Obviously, there should be some correlation between the controls that are selected to mitigate the problem associated with a specific chemical and the portion of the problem that these controls actually address. Similarly, in considering the total allowable body burden for a chemical, there should be some consistency in allocating the total among individual control measures. But can we be much more specific in generalizing approaches, say, to three of the most widely discussed toxic chemicals, namely, cadmium, mercury, and PCB's? It is difficult to identify the common aspects of cadmium-coated screws, mercury-containing dental amalgam, and polychlorinated biphenyls used in transformers, which would fit into general control strategies. Once again, at least as an interim step, I would argue for case studies as providing a background of experience in addressing future approaches to multimedia pollutants.

An Operational Early-Warning System: Is It Practical?

The need to identify and remedy problems before they take their environmental or health toll seems axiomatic. But can this be done on more than a token basis? Clearly, this question goes to the heart of this Conference.

Several approaches to problem identification seem reasonably clear:

- Gatherings of experts, such as this meeting, and also organized on an industry-by-industry basis.
- Review of past incidents to identify early-warning indicators.
- Current awareness systems to identify reported and unreported incidents involving toxic substances.
- Forecasts of market and economic trends and their impact on the future mix of products and activities of the chemical industry.

Many of you have promoted activities in these areas for some time, and we will be joining you in all of these areas in the months ahead.

What is most needed now? Better use of existing early warning systems? Bigger and better systems? More systematic orchestration of the multiple systems? I hope you will clarify these questions.

However, there undoubtedly will remain a major gap between problem identification and preventive action. Bridging this gap is particularly difficult for a bureaucracy that is basically reactive to immediate problems – and reactive in a very short-term mode. Thus, persuasive argumentation supporting the action recommended by the early warning network is essential.

Even assuming that false alarms have been separated from potentially serious problems, it will be difficult indeed to impose restrictive measures before the fact largely on the basis of unsubstantiated data. In my view, unless there is extensive cooperation on the part of industry in heeding the early warning signals – cooperation reflected in a great deal of restraint on a voluntary basis – the products of the best conceived early-warning systems are not likely to make a major impact on more than a small handful of a much larger array of potential problem substances.

THE CHEMICAL INDUSTRY AND POLICY ISSUES

The industrial representation at this Conference is encouraging. Indeed, in recent months a number of companies have shown considerable leadership in enhancing product safety, in improving the environmental compatibility of manufacturing processes, and in expanding R and D efforts to further clarify the risks of chemical activities.

For our present purposes we are interested principally in those manufacturers and processors who introduce chemical changes into their products. The following characteristics of this sector of industry – excluding the food, drug, cosmetics, and pesticides segments – seem particularly relevant:

- The annual value added to products is in the range of $110 billion, about double the level ten years ago.
- About 20,000 chemical products are in commerce with an additional 500 chemicals being added annually.

- More than 80 percent of sales is concentrated in several dozen companies but there are hundreds of additional small manufacturers.
- A large percentage of net income – ranging from 20 to 50 percent – is usually reinvested in R and D.

A number of policy considerations of particular concern to industry permeate a regulatory approach to this sector of industry, from early warning to restrictions. Some of these concerns are:

- The disincentives to R and D inherent in some types of regulatory actions could blunt the technological thrust of the industry.
- The configuration of the industry (e.g., large and small manufacturers, specialized and diversified firms) could be affected by regulatory actions which are more painful to certain types of companies.
- Regulatory actions undertaken unilaterally by the United States could affect the competitiveness of our products at home and abroad.

This does not mean that environmental actions should not affect economic interests, for environmental control is not free. However, we should recognize that individual actions – and also aggregated actions – can have many secondary and tertiary effects which may be far more significant than the more obvious primary effects. The key question of course is whether the environmental gains from regulatory actions are commensurate with any adverse economic and social impact – a question that is easy to ask but difficult to answer. In any event, we must treat early-warning signals in a responsible fashion lest the potentially affected parties seek to bury the signals out of concern that they will not be handled responsibly.

LOOKING AHEAD

Clearly Washington's preoccupation with non-environmental issues will continue to detract from the high level attention devoted to toxic substances in the months ahead, particularly on Capitol Hill. For some of the newer programs this may be a fortuitous development which will allow us to do a better job in planning long range activities, even though all of us would like to move ahead with operational activities.

During 1974 we should continue to press forward vigorously on all fronts, recognizing that regulatory actions will be more difficult amidst the general skepticism as to the importance of environmental control being expounded in some quarters. There is no reason, however, why we should not make great strides in many of the essential supporting activities. There is general agreement on the importance of increased efforts to clarify the need for, character of, and impact resulting from steps to prevent and mitigate environmental problems. Thus, I would characterize 1974 as a year of transition – a year between a period of talk and rhetoric about the need for new regulatory approaches to reduce risks associated with toxic substances and a period of accelerated action to address these risks. 1974 should be a year of coalescing ideas and energies, a year of engaging all the affected parties, and a year of setting the stage for a sensible long-term effort in dealing with multimedia pollutants.

In future years, more chemicals will be in commerce, the properties of many chemicals will be better understood, and consequently the list of chemicals considered to be hazardous to man and the environment will undoubtedly be much longer. Also, improved research and analytical capabilities will show that the effects of these chemicals – acting individually and synergistically – are much farther reaching than currently suspected effects.

Even though in a few years the emission stacks and effluent pipes will be largely plugged, and hopefully sensible land disposal of hazardous wastes will be required, more people will be exposed to more chemicals in more situations – exposure from contaminants, non-point sources, direct product contact, and generally unattributable buildup of chemicals in the environment. I am confident that society can develop the necessary precautionary measures that will limit exposure to chemicals when necessary, but not unnecessarily curtail commercial activities.

There is, of course, a danger that society will not act responsibly in anticipating and remedying toxic substance problems through its governmental and other institutions, with the inevitable outcome of endless legal confrontations. The entire approach to toxic substances could become bogged down in the courts – which would be a tragedy for us all.

Thus, the challenge to early warning is clear. It is a challenge that will

- Prioritize and focus the concerns of Government and of society on those chemical/biological interactions that require particular scrutiny in the months and years ahead;

- Provide the time needed for sluggish governmental, industrial, and commercial mechanisms to take almost unprecedented anticipatory actions; and

- Instill a sense of public confidence that the products of chemistry – both new types of goods and substitute materials for rapidly dwindling natural materials – can be made compatible with an increasingly fragile biosphere.

REVIEW OF HEALTH/ENVIRONMENTAL SYSTEMS WITH POTENTIAL EARLY WARNING APPLICATIONS

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ABSTRACT

This paper summarizes a study performed for EPA's Office of Toxic Substances on the state-of-the-art of systems, either existing or conceptual, that can be used or adapted for use to select, assess, and prioritize chemicals for their health or environmental effects. It is found that, while numerous systems can be identified, none have been formulated with sufficient breadth to permit accomplishing all these functions in a comprehensive manner.

Effective combinations of limited scope systems have been assembled by Federal agencies to achieve the chemical identification/assessment/prioritization functions needed for such public concerns as the work-place environment; human health (cancer, child poisoning, birth defects); air, water, and land contamination; and consumer-product hazards. Examination of the operational basis of a number of the individual systems within these combinations suggests that all are variations of a relatively few number of approaches to chemical selection. Three approaches for a prioritization/evaluation system are condensed from this examination.

INTRODUCTION

Our present systems for monitoring the hazards of newly introduced toxic chemical substances are inadequate. They may deal with substances after their use in products is widespread. Revelations concerning an environmental or health hazard are often made haphazardly, accidentally, or simply too late. Frequently, the indicators are there but systematic exploration of the implications of the initial findings is not accomplished.

Public concern over DDT, cyclamates, mercury, and numerous other chemical substances which have crept into the environment through technological advancement has clearly indicated the need for improved early detection, assessment, warning, and corrective measures with respect to the misapplication of intrinsically toxic substances. This identified need could be satisfied through the establishment of an early warning system for toxic chemicals. Ideally, an early warning system would provide hazard predictions which are (1) thorough or all-encompassing with respect to potential sources, (2) discriminating through reference to indicators of potential hazards, (3) adaptable to current usage, i.e., within the framework of existing technology and societal systems, and (4) amenable to the establishment of priorities for the identified substances.

The Environmental Protection Agency, through its Office of Toxic Substances (OTS), contracted with Battelle's Columbus Laboratories to identify and evaluate systems which could be adapted by EPA's Office of Toxic Substances to identify, assess, and prioritize chemicals or classes of chemicals with respect to environmental and health hazards. A major premise of the study was that systems or methodologies do exist which, if modified and/or redirected to the selection and hazard evaluation of chemicals or classes of chemicals, would provide a stepping stone toward satisfying the needs of an early warning system. Specific questions raised by OTS were these:

(1) How can a given system select both chemicals and classes of chemicals that are hazardous to man and his environment?

(2) How can a given system preselect chemicals not already in use, before they become widely dispersed and more difficult to control?

(3) How can a system select chemicals based on the potential hazard of their degradation products or their synergistic properties?

(4) How should the system consider hazards to plants, animals, and nonliving environment?

RESULTS

In the performance of this study, a literature and state-of-the-art search was made to identify systems – either in use or only conceptual – in two general areas of societal activity: health planning (including environmental, occupational, and general health) and environmental management. The term "system" was broadly defined to include not only formalized organizational structures, models, methodologies, but also less formal tools, methods, working groups, etc., which have been conceived, formulated and applied to the identification, prediction, assessment, or prioritization of chemical substances or effects. A variety of activities comprised the total information gathering effort, including manual and automated literature searches and personal contacts.

Identified Systems and Their Classification

In this study a great many systems have been identified which singly or in combination provide some of the functions desired in the selection of chemicals with respect to their hazards to man and the environment. Nearly all of these do so within a limited domain of concern, i.e., the workplace, the air, water or land environment, an ecosystem, or an aspect of human health (cancer, poisoning, aging, birth defects). From the standpoint of the mission an agency like EPA's Office of Toxic Substances, this diversity of systems represents an asset, one to be capitalized upon in seeking the identification and hazard evaluation of chemicals for which regulatory actions ought to be imposed. Conversely, this same diversity complicates the problem of effectively gaining access to all the data necessary to provide a regulation which properly balances public risk, cost, and benefit.

Table 1 lists a number of systems which were identified in the course of this study. These are described further in Battelle's final report to EPA.(1)

It has been found useful to separate the identified systems into two major categories depending upon whether their principal purpose was to identify or evaluate environment or health stressors either prior to general exposure of the public and environment (Category I) or after widespread exposure or use occurs (Category II). The first category was referred to as input surveillance (and assessment) and

TABLE 1. IDENTIFICATION/ASSESSMENT SYSTEMS

System Identifer	Sponsor	Category IA	IB	IIA	IIB
(1) Carcinogen Screening	International Agency for Research Against Cancer		X		X
(2) Animal (Rat) Toxicity Test	Center for Disease Control	X		X	
(3) Short-Term (Hamster) Cancer Test	National Cancer Institute	X			
(4) Biological Materials Surveillance	Bureau of Biologics, Food and Drug Administration	X			
(5) Surveillance of Poisons	National Clearinghouse for Poison Control, Food and Drug Administration		X		
(6) Radiological Product Surveillance	Bureau of Radiological Health, Food and Drug Administration		X		
(7) National Evaluation of X-Ray Trends	Ditto		X		
(8) Biologics Licensing	Department of Health, Education, and Welfare		X		
(9) Drug Surveillance	Bureau of Drugs, Food and Drug Administration		X		X
(10) Chemical Hazard Identification	National Cancer Institute			X	
(11) Poison Control Centers	State Departments of Health			X	
(12) Epidemic Intelligence Service	Center for Disease Control			X	

TABLE 1. IDENTIFICATION/ASSESSMENT SYSTEMS (Continued)

System Identifier	Sponsor	Category IA	 IB	 IIA	 IIB
(13) National Electronic Injury Surveillance System	Consumer Product Safety Commission			X	
(14) National Surveillance Network - National Occupational Health Survey	National Institute of Occupational Safety and Health			X	
(15) Toxic Substance List	Ditto			X	X
(16) Prioritization of Workplace Chemicals	"				X
(17) Hazard Evaluation Program	"				X
(18) Walter Reed Disease Forecasting System	U.S. Army				X
(19) Community Health Effects Surveillance Studies	Research Triangle Park, Environmental Protection Agency				X
(20) Cancer Surveillance, Epidemiology and End Results Reporting Program	National Cancer Institute				X
(21) Subclinical Toxicity Survey	Center for Disease Control				X
(22) Technical, Intelligence, and Project Information System	(Conceptual)	X	X		
(23) OVERVIEW System	Ditto		X		X
(24) National Emissions Data System (Air)	Environmental Protection Agency		X		

TABLE 1. IDENTIFICATION/ASSESSMENT SYSTEMS (Continued)

System Identifier	Sponsor	Category IA	 IB	 IIA	 II
(25) General Point Source File (Water)	Environmental Protection Agency		X		
(26) International Decade of Ocean Exploration	National Science Foundation			X	
(27) Marine Resources	National Oceanic and Atmospheric Administration			X	
(28) National Stream Quality Accounting Network	U.S. Geological Survey			X	
(29) International Biological Program	National Science Foundation			X	
(30) SAROAD	Environmental Protection Agency				X
(31) STORET	Ditto				X
(32) Environmental Monitoring	Council on Environmental Quality			X	
(33) National Fuels Surveillance Network	Environmental Protection Agency	X			
(34) Wiswesser Line Notation		X			
(35) Environmental Information System Office	Oak Ridge National Laboratories			X	X
(36) OHM-TADS	Environmental Protection Agency			X	X
(37) National Pesticides Monitoring Program	Interagency		X		X
(38) Priorities for Synthetic Organic Chemicals	Syracuse University Research Corporation				X
(39) Toxicology Information Program	National Library of Medicine		X		X

the latter as output surveillance. Each of these categories can be further subcategorized depending on whether the system activity is primarily related to identifying the existence of a possible health or an environmental stressor. In Table 1 the identified systems are listed along with a judgment regarding their appropriate categories formulated according to the following scheme:

- I. Input Surveillance
  - A. New Stressor Identification
  - B. Hazard Assessment of Recognized Stressors
- II. Output Surveillance
  - A. New Stressor Identification
  - B. Hazard Assessment of Recognized Stressors

One large class of systems identified in this program is the information repositories or data banks, some automated for storage and retrieval, others simply collections assembled in one location. Table 2 lists a number of these selected from an initial list of approximately 650 information centers in the United States.(2) The list, not meant to be complete, is divided into groups with or without computerized access and further as primarily chemical, medical, or general sources of information. The listing suggests that considerable amounts of information for chemical identification or assessment purposes are available. The problem is to determine what is available, its form, and its accessibility for identification/assessment purpose. More extensive examination of these type systems was felt beyond the scope of this study.

System Identification, Prioritization, and Evaluation Functions

While systems of Table 1 are primarily those used by governmental agencies in the health and environmental areas, there are probably as many industrial and private systems that could be identified. For example, it became apparent during the study that even a public-interest group, such as the Center for Science in the Public Interest, can function as a system for alerting the public to the hazards of toxic substances. The larger industrial chemical firms undoubtedly have internal systems for the identification and assessment of new chemical hazards.

A sufficient number of system types has been identified in this program to provide convincing evidence that

(1) No system exists which in itself will accomplish all the selection and assessment functions for toxic chemicals implied in the questions posed by OTS. A few provide some of these functions in limited areas, such as carcinogenic, workplace, or environmental hazards. A basis for adapting these including all functions (such as assessing synergistic effects) is not readily apparent.

(2) While many additional systems could be identified through continued search efforts, it is believed that these would turn out to provide essentially the same general functions as those reported in this study. In general, these functions include surveillance, surveying, monitoring, screening, reporting, sampling, testing, data compilation, or manipulation, etc., for identification, assessment, or prioritization purposes.

These observations will become clearer upon further examination of some underlying commonalities and differences between the various system methodologies.

Commonalities and Differences of Identified Systems

In studying the identified systems, some underlying commonalities of methodology were recognized. For example, the scope of the existing systems directed at chemicals is without exception more specific than the perceived needs of OTS. Existing systems have their scope limited by:

(1) class of chemicals
(2) the source of chemicals
(3) the transport media leading to exposure, and/or
(4) the affected species.

In addition, existing systems focus implicitly upon acute rather than chronic effects, due mainly to the orientation of published literature towards acute effects. Thus, while the systems identified might be recognized as partial solutions to OTS' needs, the expansion of the scope of any existing system is obviously not easily accomplished.

Another area of commonality lies within the goals of existing systems. Almost every system studied has as a basic goal the determination of a potentially hazardous subset of chemicals or chemical classes from a larger list of candidates. This process may be accomplished in a single step, or a hierarchy of steps may be employed, with each step again consisting of the determination of a potentially more hazardous subset.

Each step may be viewed as a process in which information is gathered for the list of chemical candidates and combined in some manner to produce an assessment of the estimated hazard on a univariate scale. The utilization of judgment to provide a true/false answer to the question of hazard is an example of the combination/assessment process.

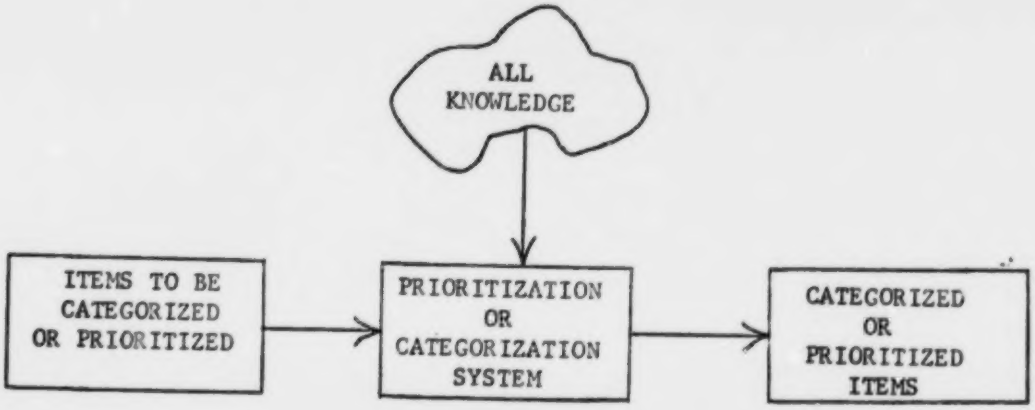
The original step of the hierarchy does not have a preceding step to provide a candidate list. Many existing systems have developed sensor networks to generate the chemicals on the original candidate list. One frequently employed sensor network for existing systems is the use of the literature, i.e., either monitoring the raw literature or condensations of literature. The NIOSH Toxic Substances List(3), for example, relies upon Chemical Abstracts as a source of chemical names and information. Further information needed for the list is obtained from the open literature. Some systems studied, however, relied upon previously published candidate lists, hence the first step had been previously accomplished for these systems. Another example of a sensor network for the generation of an original candidate list, typified by the approach used by the National Pesticide Monitoring Program, was the collected judgment of professionals, queried and resolved by the Delphi technique. This approach is feasible when the candidate list is relatively small.

Some "sensor" networks are monitoring networks in the real environment. The NIESS system of the Consumer Product Safety

Commission, for example, generates its candidate list for hazards from hospital emergency room reports. This approach is useful when a direct, measurable cause-effect result can be observed after the fact.

After their sensor networks establish candidate lists of chemicals, existing systems determine a potentially hazardous subset of chemicals through a single or repeated application of information collection and decision making. The large number of sources of chemical information was referred to earlier (Table 2).

After the information is collected, existing systems manipulate the information to form a design basis by which prioritization/classification decisions can be made. A general framework has been structured which expresses the design basis of most existing prioritization systems. This general basic system for prioritization or categorization accepts from the universe of knowledge a small subset of information. This information subset is then processed and combined to produce categories or priorities. Graphically, the process is as follows:


ALL KNOWLEDGE
ITEMS TO BE CATEGORIZED OR PRIORITIZED
PRIORITIZATION OR CATEGORIZATION SYSTEM
CATEGORIZED OR PRIORITIZED ITEMS

To design or adapt a prioritization/categorization system, it is necessary to specify

(1) The subset of information to be used by the system

(2) The algorithm by which the subset of information will be manipulated and combined.

TABLE 2. CHEMICAL TOXICITY DATA SOURCES

A. Sources with Automated Storage and Retrieval Facilities

Chemical

- Sadtler Research Laboratories, Inc.
- American Chemical Society
- Columbia University RADICAL System
- Commission of the European Communities - ECDIS

Medical

- University of Rochester
- North Carolina State University
- Midwest Research Laboratories
- National Library of Medicine
- Biological Abstracts

General

- The John Crerar Library
- Argonne Code Center
- Battelle Memorial Institute (Columbus and Northwest)
- Atomic Energy Commission - Division of Technical Information Extension
- Nuclear Safety Information Center
- Pesticides Information Center

B. Other Information Centers

Chemicals

- Household Substances Data File, FDA
- The Soap and Detergent Association
- American Petroleum Institute
- Industrial Hygiene Foundation of America, Inc.
- Tobacco Literature Service

Medical

- National Center for Chronic Disease Control
- Army Munitions Command - Toxicological Information Center
- New York Academy of Medicine
- National Clearinghouse for Poison Control
- Pharmaceutical Information Service
- Pharmaco-Medical Documentation

General

- International Association of Water Pollution Research
- National Academy of Science-Engineering
- World Life Research Institute
- Institute for Scientific Information

Examination of the existing systems suggests three approaches to the design of a prioritization/categorization algorithm

(1) The "wise man" approach, a subjective design where the system framework is established on the basis of perceived needs and an assessment of available resources. The National Pesticide Monitoring Program, and many contemporary systems appear to have been formulated this way.

(2) The "index" approach, a design based upon a specific ranking parameter formed algebraically and/or logically from other data. This would be exemplified by a system for ranking hazardous waterborne substances by the volume of water necessary to dilute expected annual spillage to a safe or limiting concentration.(5)

(3) The "optimized" approach, designs wherein the parameters are selected for producing categories or priority ranking on the basis of assigned values and weightings. This was the technique employed, e.g., in the Coast Guard's Chemical Hazard Ranking Information System (CHRIS).(6)

A structure for classification of existing systems by utility and a structure for classification by design of the prioritization/categorization system have been presented. A representative sample of existing systems within the framework of these structures is presented to illustrate the structure.

"Wise Man" Approach

A classic example of the wise man approach is given by the National Pesticide Monitoring Program. The NPMP consists of an integrated interagency effort to restrict, control, and monitor the pesticides and their decay products in the environment. The program consists of three basic functions.

(1) Criteria – developed by published information, company data, brainstorming

(2) Registration – to control the quantity of pesticides entering the environment

(3) Technical Services – to develop monitoring techniques and to coordinate the efforts of the many environmental monitoring programs currently in existence.

The program is structured around a list of pesticides and trace metals. The list was constructed via a collective set of opinions, based on toxicity, quantity, and persistence. Local monitoring programs are free to exercise their own judgment on which pesticides are monitored.

"Index" Approach

An index can be constructed by two methods. In a stochastic construction, statistical techniques are used to derive indices from a wide variety of data or observations. A large amount of data is generally required for the stochastic approach. The deterministic construction identifies or deduces (subjectively) relevant indices from the area of concern. The indices may be algebraic and/or logical combinations of data. Frequently an index may have a physical meaning.

Stochastic Index. In 1971, Synectics Corporation developed a system for industrial waste treatment RD&D project priority allocation. In this study, three priority indicators were derived by the stochastic technique from existing, implicit EPA priorities.

Each of the indicators was derived by the utilization of past Federal funding to provide rank order as a dependent variable. The independent variables for the three indices (location, constituent, and industry) are presented in Table 3. A statistical technique was used to derive the three indices from the gathered data. These indices were then utilized to prioritize future EPA expenditures by state and by industry.

The scheme presented by Synectics typifies the construction of a stochastic index to perform prioritization. The data utilized to construct the index (Federally funded), however, must be viewed as subjective data representing at best the consensus of experts.

Deterministic Index. Many examples of deterministic indices are available. One such study was performed by Battelle for the Consumer Protection and Environmental Health Service (CPEHS)(4), later separated into two agencies, and ultimately disbanded. A conceptual system was derived to examine research and development program planning needs, and to develop a management assistance program. The study itself can be categorized into the II. B category of Table 1, while the prioritization scheme is based on a deterministic index.

Problem identification from the perspective of environmental stressors and priority setting were determined to be important functions to be performed in the planning cycle. No single method for planning and priority setting was found to be totally applicable to the mix of complex problems encountered by CPEHS. Continuation of categorical planning activities was recommended to serve as the foundation for the development of an integrated planning system based upon quantitative assessments of the impact of technology upon man and his environment. Full implementation of the integrated planning system requires the availability of a hierarchy of mathematical models for the assessments.

Demonstration of the integrated planning system concept was provided through case studies for lead and DDT, and for lead, a preliminary identification of elements to be included in a partial program plan was made.

The concept of Urgency as a means to establish priorities for EHS was investigated. The Urgency consists of the people affected, the severity of the effect, and the rate of change of these quantities with time.

A priority index was formed based upon the average Urgency value during a planning horizon, where Urgency was defined as the product of severity and population at risk. The calculation of Urgency can be weighted and summed over each population at risk to provide an estimate of total Urgency. It was illustrated that Urgency could be discounted in time.

As the study did not have the data to perform priority ranking, and such data would not be available to CPEHS for several years after implementation, the ranking was never performed. An intermediate alternative method was proposed, however. This was in essence a "wise man" approach, utilizing value judgments from experts.

TABLE 3. INDEPENDENT VARIABLES FOR STOCHASTIC INDICES IN EPA PRIORITIZATION OF FUNDING

Locational (State as Case)	Effluent Constituent (State as Case)	Industrial Volume (SIC 2-Digit Code as Case)
Industrial waste-water volume	Effluent volume	Industrial effluent volume
Population	State standard	Water use
Valve added by manufacturer	Economic effects	Valve added by manufacturer
Annual runoff	EPA regional standard	Employment
Water area	Public notice	Number of states with plants
Population density	Low concentration limit	Total plants
Industrial water use	High concentration limit	Plants using >20 mgy
	Relative cost of removal	

Other examples of deterministic indicators are available. These include

(1) A water hazard ranking scheme (Figure 1) which utilizes volume transported, accident probabilities, and critical concentrations to provide a rank based upon the expected volume of water polluted to the critical concentration annually.(5)

(2) A solid waste hazard screening system (Figure 2) which classifies a material as very hazardous if the material meets any one of eleven criteria. This is an example of a logical (as opposed to algebraic) indicator.

(3) An air hazard ranking scheme analogous to (1) above, but including stationary sources. Stationary sources produced an index based upon a record of accidents with arbitrary scoring, while mobile sources produced an index analogous to (1) above, but with considerations of volitility and hazard ratings. The two indices were combined logarithmetically to produce a hazard ranking index, for accidental air pollution episodes.

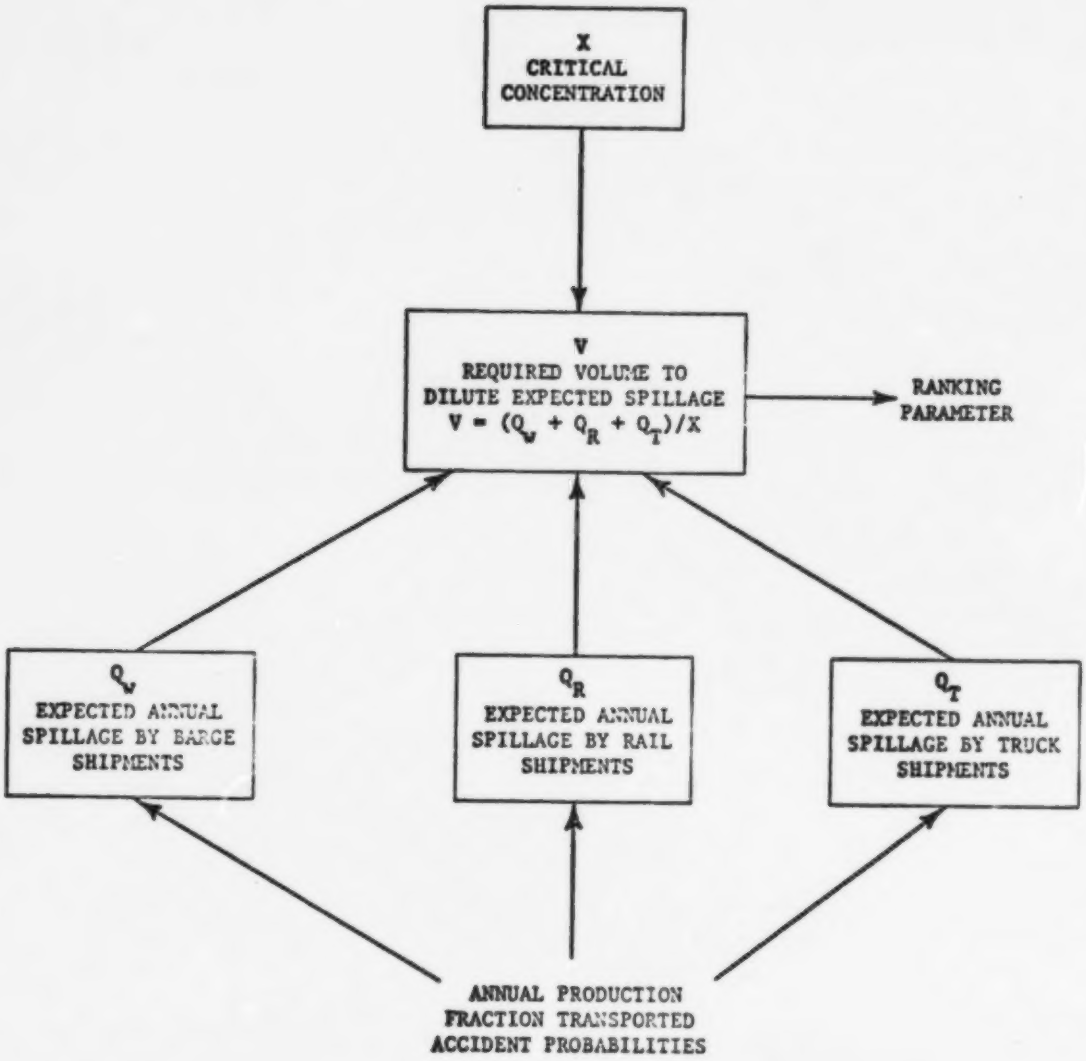

X
CRITICAL
CONCENTRATION
V
REQUIRED VOLUME TO
DILUTE EXPECTED SPILLAGE
$V = (Q_W + Q_R + Q_T)/X$
RANKING
PARAMETER
Q_W
EXPECTED ANNUAL
SPILLAGE BY BARGE
SHIPMENTS
Q_R
EXPECTED ANNUAL
SPILLAGE BY RAIL
SHIPMENTS
Q_T
EXPECTED ANNUAL
SPILLAGE BY TRUCK
SHIPMENTS
ANNUAL PRODUCTION
FRACTION TRANSPORTED
ACCIDENT PROBABILITIES

FIGURE 1. GRAPHIC REPRESENTATION OF HAZARDOUS WATERBORNE SUBSTANCES MODEL

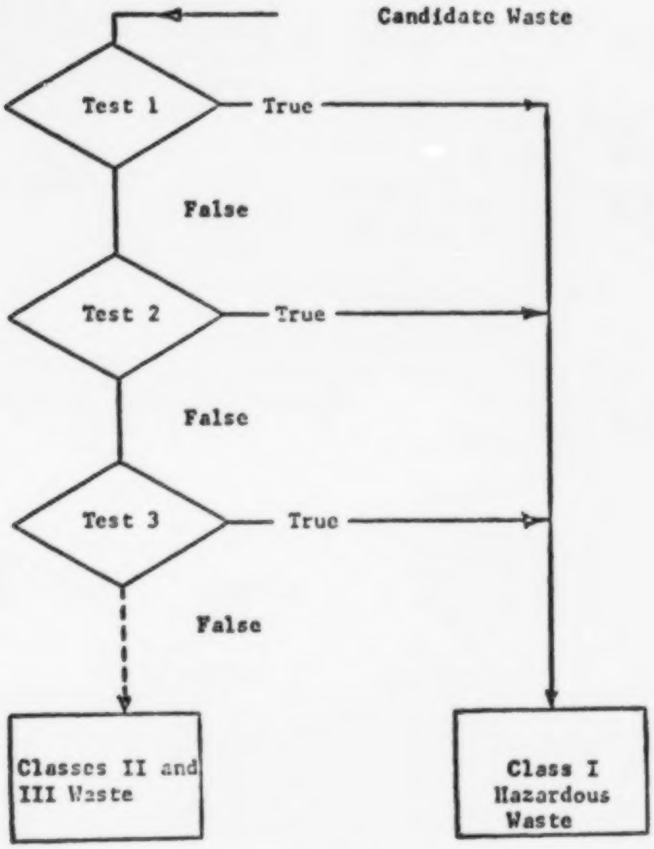

Candidate Waste
Test 1
True
False
Test 2
True
False
Test 3
True
False
Classes II and III Waste
Class I Hazardous Waste

FIGURE 2. GRAPHIC REPRESENTATIVE OF THE HAZARDOUS WASTE DECISION MODEL

(4) The Office of Water Programs has developed a list of hazardous substances based upon a logical deterministic index. Data considered include half-life, bioconcentration, radiotoxicity, lethality (in aqua, oral, dermal, vapor), oxygen demand, and nuisance aquatic growth stimulation.

(5) NIOSH provides each year a priority list for Criteria Development for Toxic Substances and Physical Agents. The 1972 list was based upon a system developed by the staff of the former Bureau of Occupational Health and Safety. Five indicators, namely

(a) Population at risk, based on walk-through surveys of industrial work forces

(b) Relative toxicity, a rank score based upon expert opinion

(c) Incidence of disease, from occupational records

(d) Quantity of production

(e) Trend of production quantity were combined to produce an index of priority.

The 1973 priority list was obtained in a similar manner, except that the indicators were slightly different. The population at risk, quantity of production, and trend were combined to produce expected exposure for a given time frame. The relative toxicity and disease incidence items were discarded in favor of a subjective assessment of the combination of likelihood of disease and severity, derived by a Delphi technique from the opinions of fifty occupational health professionals.

"Optimized" Approach

The Coast Guard CHRIS system is an example of the optimized approach. The CHRIS (Chemical Hazards Response Information

System) study was performed by A. D. Little, Inc., in 1972, to provide a response system to the spillage of hazardous waterborne materials.(6)

The study contains an analysis of information requirements for the five stages of a spillage incident, namely

(1) Detection, evaluation, notification
(2) Containment and countermeasures
(3) Cleanup, disposal
(4) Restoration
(5) Adjudication.

A tentative list containing some 144 perceived information needs was generated (a laundry list). This list was truncated to 78 elements by subjective elimination and aggregation. The list then contained eight major categories:

(I) Chemical (16 elements)
(II) Shipping and Carrier (8 elements)
(III) Environment (16 elements)
(IV) Resource (8 elements)
(V) Incident (13 elements)
(VI) Procedures and Background (4 elements)
(VII) Hazard Evaluation (7 elements)
(VIII) Response Model (6 elements).

Nine categories of information users were defined, as were three actions of users and four media by which information could be provided.

Subjective analysis then provided further variables. A score of 0 to 5 was provided as a consequence of a wrong decision by each of the nine users based on each of the 78 information elements. An incremental reduction in the likelihood of the wrong decision by each of the nine users due to the provision of each information element was subjectively assessed. A weighting factor was provided to modify the consequence of each wrong decision by the action of the user. A RCR score (Risk Consequence Reduction) was then computed for each information element – user pair.

In this manner the information needs of CHRIS were prioritized. It was found, for example, that the top nineteen information elements provided a 50 percent reduction in RCR. The most critical information elements for each phase could also be determined with this technique. It should be emphasized, however, that the prioritization is based upon subjective data.

Prioritization in Early Warning

Many existing systems for identifying and evaluating chemicals which are potentially hazardous have been identified. An improved early warning system would incorporate many of these existing systems as components, but the specific form of the early warning system will be at least partially dependent upon the prioritization or screening of chemicals which must take place before committing resources to detailed assessment of toxic hazards.

The state of the art of prioritization schemes for hazardous chemicals has been shown to be quite limited. In short, these limitations include

(1) The liberal utilization of subjective data
(2) The availability of only three algorithms for prioritization.

As the state of the art of prioritization is limited, so must be its application to an early warning system. Within these limitations, it is fairly straightforward to devise prioritization schemes for an early warning system.

Three approaches for prioritization of chemicals and classes of chemicals, covering the range of the state of the art, are discussed here. These are presented with the recognition that perfect screening is impossible, that much data (particularly for new compounds) may be missing, and that the screening process must be relatively simple if it is to be applied to a large number of chemicals.

The first would utilize the wise man approach as, for example, used in the National Pesticide Monitoring Program. A list of candidate chemicals would be derived from the consensus of informed experts. The list of experts should be quite large, as many disciplines should be represented. The effort to generate the original list would be large, but the list could be periodically updated for far less effort. The resulting list would be, in essence, completely subjective.

The list of chemicals to be screened would not be formal. Rather, it would be encumbent upon the experts to provide "pre-screened" compounds (for judgment by the consensus) from the literature available to the experts. It would be desirable to provide an adequate data base for utilization by the experts throughout the screening process.

In the second approach, an index could be constructed to perform prioritization. Such a technique applicable to organic chemicals based on a stochastic index has been proposed(7): it could be extended to others. The variables of the index would be selected subjectively. The difficulty with this approach is that an index which allows screening with a degree of reliability would require data that is unavailable for many of the chemicals to be screened. The subjective data required for the screening may weaken the reliability of the results.

If a stochastic index is constructed it may be desired to construct indices on subsets of the independent variables. For example, a discriminant analysis for screening variables might be performed for the entire set of independent variables as well as subsets. Discriminant screening of chemicals with missing data would then require the application of the discriminant function appropriate to the available data. Needless to say, a significant amount of data from case studies would be required to derive stochastic indices.

In the third approach, a detailed laundry list of desired information for screening would be considered. A scheme would be derived to evaluate the worth of each element to the screening process, considering the cost of errors in an early warning system, as well as the cost of obtaining the information. In this manner the most cost-effective information elements for a screening process would be derived. The information items could then be combined as in the second approach to perform the screening.

CONCLUSIONS

Numerous systems exist which have as their objective the identification of adverse chemical effects on human health and/or the environment. Nearly all have been formulated within a relatively narrow framework of applicability or use; as such, they are not readily adaptable to the needs of EPA's Office of Toxic Substances (OTS). Nevertheless, many of these systems could represent important adjuncts to any OTS efforts to monitor public exposure to various chemicals. For example, many of these systems have well established sensor networks which are valuable early indicators of problem substances.

Existing systems can be classified in several ways. Early in the program it became apparent that a major system class was the information repositories for chemical data – especially toxicity data. These information centers are numerous, frequently provide automated storage and retrieval, and generally have a defined albeit limited scope.

Systems other than information centers can be classified with respect to whether their principal function is to identify chemical substances before general exposure of the public and environment occurs (input surveillance), or after such occurs (output surveillance). Each of these types can be further subcategorized into those which basically seek to identify new or unrecognized chemical stressors and those which seek to evaluate the hazard of a recognized stressor.

Systems differ in the manner in which a candidate list of substances for evaluation is identified and comprise (1) systematic literature scanning, (2) licensing, (3) test protocols, (4) expert panels, (5) data base sampling, accumulation, or analysis, (6) incident reports, etc. Conversely, an examination of the design basis of existing systems suggests only a few basic approaches for assessment/prioritization (or categorization) functions. Three of these are the use of experts, a numerical index of measure or hazard, and subjective weighting factors or assigned values for selected parameters felt to be of importance.

Finally, it is possible to utilize this knowledge of existing systems to conceptualize three potential designs for a prioritization/classification scheme. As with most existing systems, the three designs rely heavily upon subjective input.

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A RESEARCH PROGRAM TO ACQUIRE AND ANALYZE INFORMATION ON CHEMICALS THAT IMPACT ON MAN AND HIS ENVIRONMENT

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ABSTRACT

SRI has developed a system to collect, analyze, and systematize information on the chemical description, production, uses and human exposure of chemicals with which the U. S. population comes in contact.

This effort provides information to aid the National Cancer Institute Carcinogenesis Program in selecting chemicals to test to which the U. S. population is exposed. The criteria used by NCI's Chemical Selection Committee for selecting chemicals for carcinogenic testing are:

- The degree of overall human exposure
- Projected new or increased human exposure
- Exposure of subpopulations important to society
- Epidemiological clues (high cancer incidence subpopulations)
- Relation to known carcinogens
- Gaps in knowledge.

The present data base contains information on 3,200 chemicals in the following categories:

Intentional food additives
Pesticide residues in food
Proprietary drugs
Prescription drugs
Cosmetics
Air pollutants
Water pollutants
Soaps and detergents
Trade sales paints

- The establishment of an "early warning" surveillance system to detect new chemicals coming into use, increased

use of existing chemicals, and new uses of existing chemicals that will lead to increased human exposure

- Breaking out estimates for present exposure categories to reflect per capita and per weight exposure estimates for important subpopulations
- Further work in representing structure-activity relationships
- Refining exposure factors used in estimating human intake
- Including data on high risk subpopulations
- Enlarging the data base to include other chemical, physical, and biological information
- Expanding the data base to include additional exposure categories and classes of chemicals
- Reprogramming the data processing system to handle a larger data base and to respond to a greater range of inquiries
- Expand the use of the system to serve an expanded set of objectives serving other groups within NCI and other agencies with regulatory and standard-setting responsibilities concerned with health hazards arising from exposure to chemicals.

These categories are subdivided into 900 product types representing 18,000 chemical-product combinations.

The data are in computer-readable form and contain the following information:

Product	Each Ingredient Chemical
Product name	CAS number and name
Quantity available for exposure	Strength (percent) in each product
Exposure routes — oral, dermal, respiratory, and parenteral	Degree of uncertainty associated with quantitative data
Exposure factor by route	References to data sources

In addition to the information on the 3,200 chemicals in the above nine exposure categories, a data bank of approximately 25,000 chemicals has been developed which includes many of the substances to which the human population is most likely to be exposed. These chemicals were drawn from eighteen recognized sources of information on such products as cosmetics, food additives, medicinals, etc. For each of the 25,000 chemicals in this data bank, the CAS number, structure, chemical name, and synonyms are stored in computer readable form.

A computerized chemical classification scheme has also been developed that contains 220 nodes or end points. This development has allowed a node assignment to be made for each of the chemicals for which exposure estimates have been made. As additional biological data become available it may eventually be possible to make informed guesses as to a molecule's carcinogenic potential based on such a chemical classification scheme.

In addition to providing the Chemical Selection Committee with information based upon the existing data base, a number of developmental tasks are either under way or under consideration including:

NATIONAL CANCER INSTITUTE PROGRAM OF CANCER SURVEILLANCE, EPIDEMIOLOGY AND END RESULTS REPORTING (SEER Program)

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ABSTRACT

The SEER Program provides information on trends in the incidence of the various forms of cancer in the United States, variation in the occurrence of cancer among different population groups and in different geographic areas, changes in diagnostic and treatment practices and the associated end results in the general run of cancer patients. Data are obtained from a selected number of population-based cancer registries that provide uniform information on a continuing basis and these registries participate in ad hoc studies designed to identify and assess etiologic and prognostic factors.

The SEER Program contributes to Objective No. 5 of the National Cancer Plan, i.e., "develop the means to achieve an accurate assessment of (a) the risk of developing cancer in groups and in individuals and (b) the presence, extent and probable course of existing cancers".

INTRODUCTION

As the National Cancer Program develops, it is becoming increasingly evident that a variety of program elements and program participants relate to and are concerned with the collection, analysis and utilization of data on the incidence of cancer, the characteristics of patients and their disease, treatment and end results. No one organization can or should attempt to exercise primary control over the broad variety of data required to meet the needs of the many participants in the National Cancer Program. However, it is highly desirable for organizations and institutions with a primary interest in data collection, analysis and utilization to be aware of one another's activities and interests.

SEER PROGRAM PARTICIPANTS

The National Cancer Institute is sponsoring a program of Cancer Surveillance, Epidemiology and End Results Reporting (SEER). This program is being coordinated by the Biometry Branch, Division of Cancer Cause and Prevention and is an outgrowth of the End Results Evaluation Program, which has been in operation since 1956, and the Third National Cancer Survey which covered the three year period 1969-1971.(1) It is designed to support the National Cancer Plan and help achieve Objective Number 5 which is to "develop the means to achieve an accurate assessment of (a) the risk of developing cancer in groups and in individuals and (b) the presence, extent and probable course of existing cancers".

The SEER Program involves the collaboration of two types of participants:

(a) Population-Based Tumor Registries
These registries have reporting systems designed to obtain information on every newly diagnosed case of cancer (except nonmelanotic skin cancer) and on every death with cancer, among members of a defined population, usually one to three million people. The cooperation of every general hospital and of the state office of vital statistics is necessary to assure completeness of reporting.

The goal is to produce reliable and timely data on the incidence of cancer among the residents of the area to provide information on changes over time and on variation in the occurrence of cancer among subgroups of the population.

All, or a majority of the hospitals, participate in a patient follow-up system to provide information on end results, i.e., the relationship of patient survival to the characteristics of the patient, the nature of the tumor, extent of disease at diagnosis, and treatment.

The collected data are utilized to identify issues that warrant investigation through special studies, which may be carried out within a single geographic area or as a collaborative project in two or more areas.

In selecting areas for inclusion in the SEER Program, a number of factors are considered, including:

(1) Geographic dispersion to provide for a variety of environmental and industrial settings, and a variety of racial, ethnic socioeconomic population groups.

(2) Availability and interest of appropriate professional and technical personnel associated with an appropriate local sponsoring organization.

(3) Interest and support of the local community, including the hospitals, practicing physicians, and both public and voluntary organizations.

(b) Epidemiology Research and Training Centers
A selected number of areas with population-based tumor registries are being assisted in the development of broad programs of epidemiologic research and training. Such programs require active participation of educational institutions with senior staff experienced in planning and carrying out epidemiologic and related research in cancer and other chronic diseases. The availability and interest of specialists in a variety of medical and scientific disciplines, who will participate in different studies, is of primary importance.

A principal goal is the development of research programs that provide a means for attracting talented young people for on-the-job training in cancer epidemiology and related skills, supplemented by appropriate related academic studies.

The current participants are shown in Table 1. These nine registries cover defined populations totaling almost 10% of the United States population. A few other areas of the country are being considered, but complete coverage of the United States is not considered necessary or feasible at this time. In order to provide current data on cancer incidence, the registries will submit their incidence data for each calendar year to the National Cancer Institute annually within 12 months of the end of each year. In addition, a complete data file including current follow-up information on cases diagnosed during a specified calendar period will be submitted every two years.

Although cancer incidence statistics are not available for the entire country, complete cancer mortality data are collected by the National Center for Health Statistics and are available on an individual

TABLE 1. SEER PROGRAM PARTICIPANTS

Contract Agency	Area Covered	Population Covered - 1970
California State Department of Health	Alameda, Contra Costa, Marin, San Francisco, and San Mateo counties	3,109,519
Connecticut State Department of Health	Entire state of Connecticut	3,031,709
Fred Hutchinson Cancer Research Center	King, Kitsap, Pierce Snohomish and Thurston counties, Washington	1,934,628
University of Iowa	Entire state of Iowa	2,824,376
Louisiana Health, Social and Rehabilitation Services Administration	Jefferson, Orleans and St. Bernard parishes, Louisiana	982,224
Michigan Cancer Foundation	Macomb, Oakland and Wayne counties, Michigan	4,199,931
University of New Mexico	Entire state of New Mexico	1,016,000
Research Corporation of the University of Hawaii	Entire state of Hawaii	768,561
University of Utah	Entire state of Utah	1,059,273
	TOTAL	18,926,221

county basis. Counterbalancing the advantages of having mortality data for the entire country is the fact that the relationship between the number of cancer deaths and the number of newly diagnosed cases of cancer varies among the different forms of cancer and also by race, sex, age, socio-economic status, and calendar time. Thus, sole reliance on mortality data may lead to erroneous conclusions and invalid comparisons.

The cancer incidence data produced annually by the SEER Program will be a great improvement over that previously available. Besides the Third National Cancer Survey which covered 1969 through 1971, the only other national surveys were the two Ten Cities Surveys of 1937 and 1947.(2) The large gaps in our data base for the time intervals between surveys are filled only partially with annual data from the Connecticut Tumor Registry which started in 1935.(3) The Connecticut data have been very useful for assessing the trends suggested by the three survey data points. There is considerable interest in trends in the occurrence of cancer because of their usefulness in

(1) Identification of leads regarding the impact of changes in the environment and in human behavior,

(2) Assessment of the impact of cancer control programs, such as anti-smoking campaigns and exfoliative cytology, and

(3) Measurement of changes in the magnitude and nature of the cancer problem for planning the allocation and development of resources.

Since we have three sources of data regarding long term trends in cancer occurrence in the United States, it is of interest to see whether a consistent picture emerges and whether observed inconsistencies can be rationalized. Trends in mortality reflect the interplay of two factors, namely, the rate of incidence and the patient survival rate. The most comprehensive data available on patient survival has been compiled by the End Results Evaluation Program sponsored by the National Cancer Institute. The latest report contains survival data on more than half a million cases of cancer diagnosed during the period 1940-1969.(4) This program is now an integral part of the SEER Program.

LONG-TERM TRENDS IN CANCER OCCURRENCE

For all sites combined, different trends can be seen for males and females. Among males, both incidence and mortality have been increasing continuously since at least 1935. The increase has been particularly large among blacks, but this may be partially a reflection of improvement in the delivery of medical care resulting in more complete diagnosis of the disease. It is likely, however, that a substantial fraction of the reported increase reflects the impact of environmental factors, such as movement from rural to urban areas and concentration in inner cities, changes in occupation, and changes in eating, drinking and smoking habits. Among females, very little change can be seen for black women since 1935, but white women have experienced a slight decrease.

All measures point to large continuous increases in lung cancer, as shown in Figure 1. Over the total period from 1935 to 1970, the increase among men was much larger than among women. As a result of the sharp rise in the reported occurrence of lung cancer in the black population, the incidence rates (adjusted for age) for blacks are now higher than for whites, particularly among men.

The greatest difference in cancer occurrence between the races is in cancer of the esophagus, as shown in Figure 2. In the white population there have been minor fluctuations in occurrence over the years, but no appreciable increase or decrease. In the black population, however, sharp increases can be seen in both incidence of and mortality from esophageal cancer. As a consequence, the incidence rates in the black population are now much higher than in the white - rates of 15.1 versus 4.1 in men and 3.2 versus 1.2 in women. The extent to which the marked rise in reported incidence and mortality in the black population reflects more complete case finding due to increased availability of medical care is not known. However, it is clear that esophageal cancer is now a sustantial health problem among blacks. The decreased incidence of esophageal cancer in white men during the 1960's is intriguing and should be studied in conjunction with the continued increase in incidence among black men. Can these divergent trends be explained by the same set of factors, such as changes in occupational exposure or changes in alcohol consumption?

Figure 3 shows that all measures point to an increased trend in cancer of the pancreas, but with marked variations in magnitude. In the white population, the increases in both incidence and mortality rates were higher in men than in women. They were also higher in the black population than in the white. It seems likely that at least part of the large reported increase in the occurrence of pancreatic cancer in the black population is due to more frequent identification of the disease as a result of increased availability of medical care.

The incidence of and mortality from cancer of the uterus have decreased in both black and white women, as shown in Figure 4. The incidence data indicate a somewhat larger decrease among blacks, whereas the mortality data indicate a larger decrease in whites. The data presented pertain to all cancers of the uterus, except carcinoma in situ of the cervix. In examining trends, the

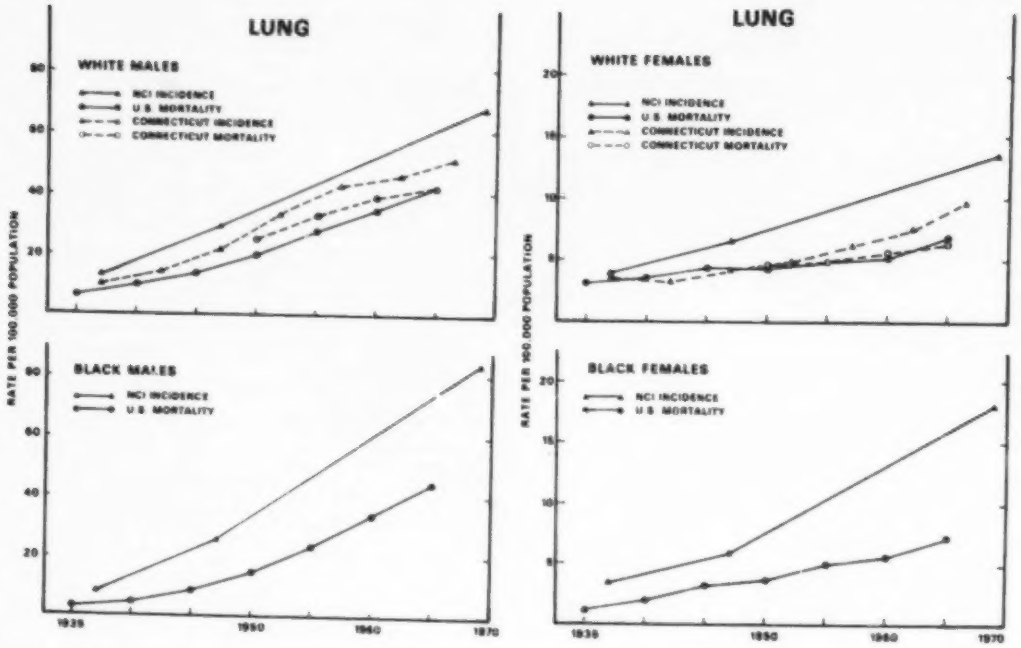

FIGURE 1. LUNG: TREND OF CANCER INCIDENCE AND MORTALITY RATES, 1935-1969 (AGE-ADJUSTED, 1950 STAMDARD POPULATION

Note: Different scales used for males and females.

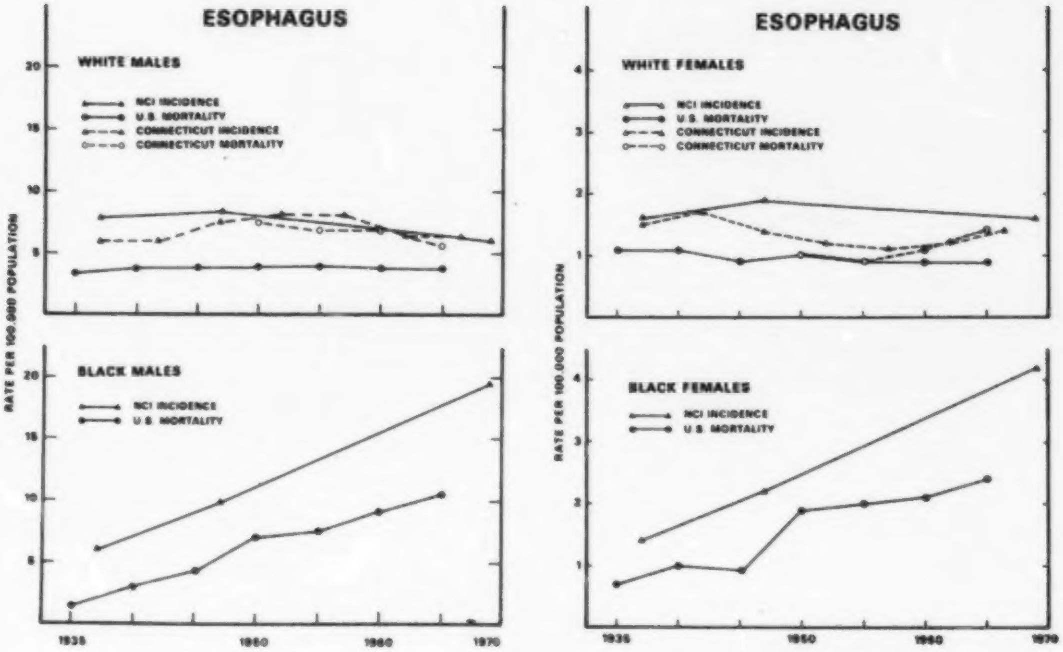

FIGURE 2. ESOPHAGUS: TREND OF CANCER INCIDENCE AND MORTALITY RATES, 1935-1969 (AGE-ADJUSTED, 1950 STANDARD POPULATION

Note: Different scales used for males and females.

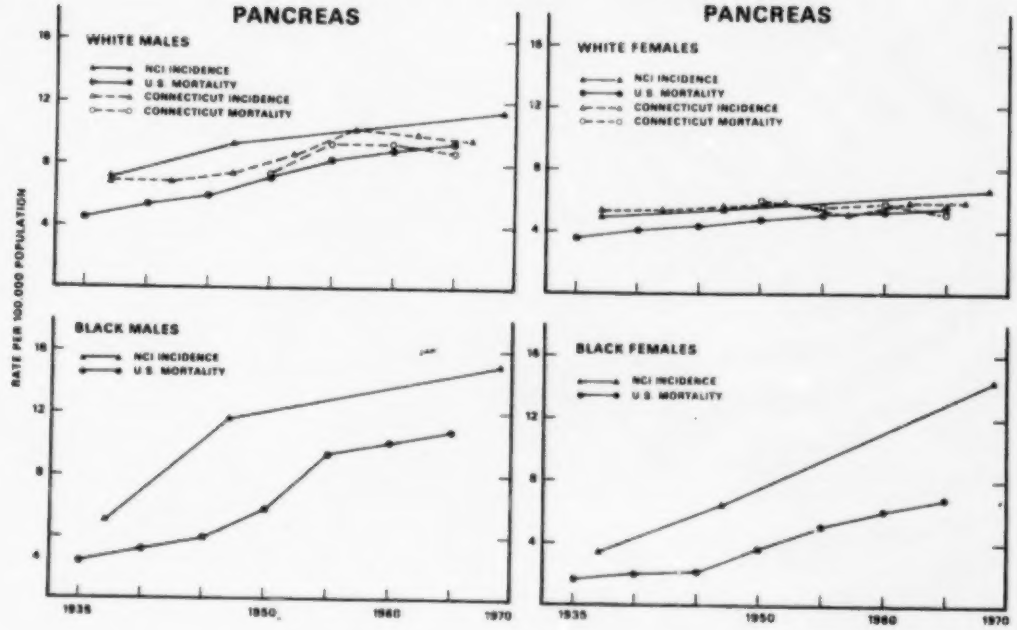

FIGURE 3. PANCREAS: TREND OF CANCER INCIDENCE AND MORTALITY RATES, 1935-1969 (AGE-ADJUSTED, 1950 STANDARD POPULATION

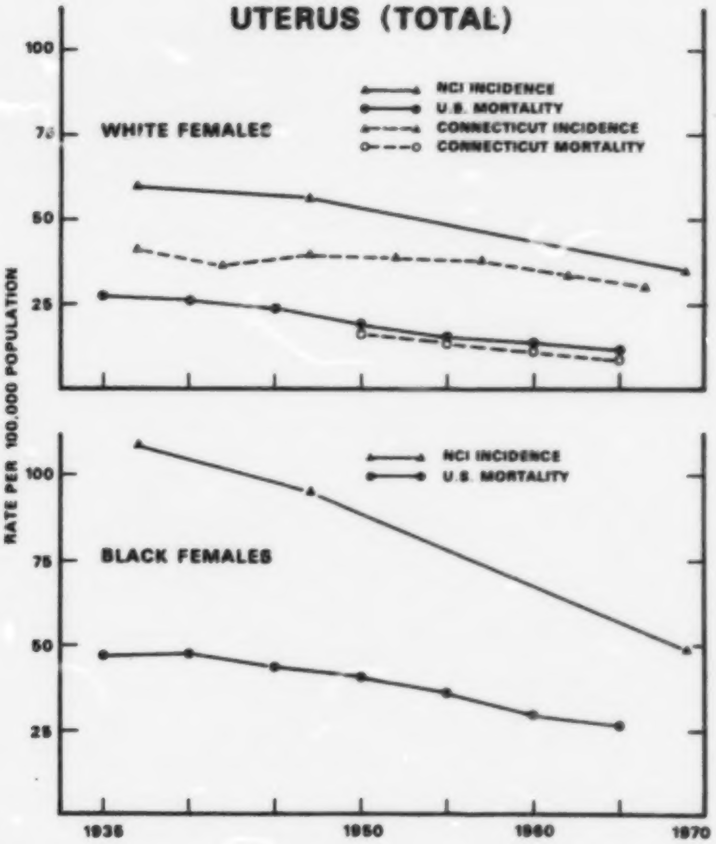

FIGURE 4. UTERUS: TREND OF CANCER INCIDENCE AND MORTALITY RATES, 1935-1969 (AGE-ADJUSTED, 1950 STANDARD POPULATION

Note: Includes invasive cancers of all parts of the uterus. Excludes carcinoma *in situ*.

data for uterine cervix and corpus have been combined because medical records often do not contain sufficiently specific information to separate them. The decreases in both incidence and mortality have been continuous since the late 1930's. Thus, the downward trend began well before the advent of cervical cytology screening programs in the mid-1950's.

Figure 5 shows the trends for cancer of the bladder. The survey data point to increases in incidence in both white and black males and decreases in both white and black females. The Connecticut data, which pertain mainly to whites, indicate increases in both sexes, but the increase in males is much larger than in females.

Present knowledge indicates that many types of cancer are associated with environmental factors, and a majority of cancer deaths is attributable to them. The estimated cancer deaths in the United States for 1973 are shown in Table 2 along with an estimate of the extent to which they are attributed to environmental factors.

TABLE 2. ESTIMATED CANCER DEATHS IN USA
FOR 1973 (BOTH SEXES)

Site	Total Deaths	Extent Attributed to Environmental Factors	
Lung	72,000	++++	Tobacco, Asbestos, Air Pollutants, Occupational
Colon-Rectum	47,400	+++	Diet, Other Environmental
Pancreas	19,200	++?	Tobacco, Diet(?)
Leukemia	15,300	+	Radiation, Chemicals
Stomach	14,700	+++	Diet, Other Environmental
Bladder	9,200	+++	Occupational, Tobacco, Diet (?) Other Environmental
Oral Cavity	7,600	++	Tobacco, Chemicals, Diet (?)
Liver (Primary)	7,200	++	Diet, Other Environmental
Esophagus	6,400	++	Environmental
Skin	5,200	++++	Ultraviolet Light, Chemicals, Occupational
Larynx	3,000	+++	Tobacco, Air Pollutants
Total These Sites	207,000	+++	
Other Sites	143,000	+, ?	(Includes Hormonal Factors)
TOTAL All Sites	350,000	++	

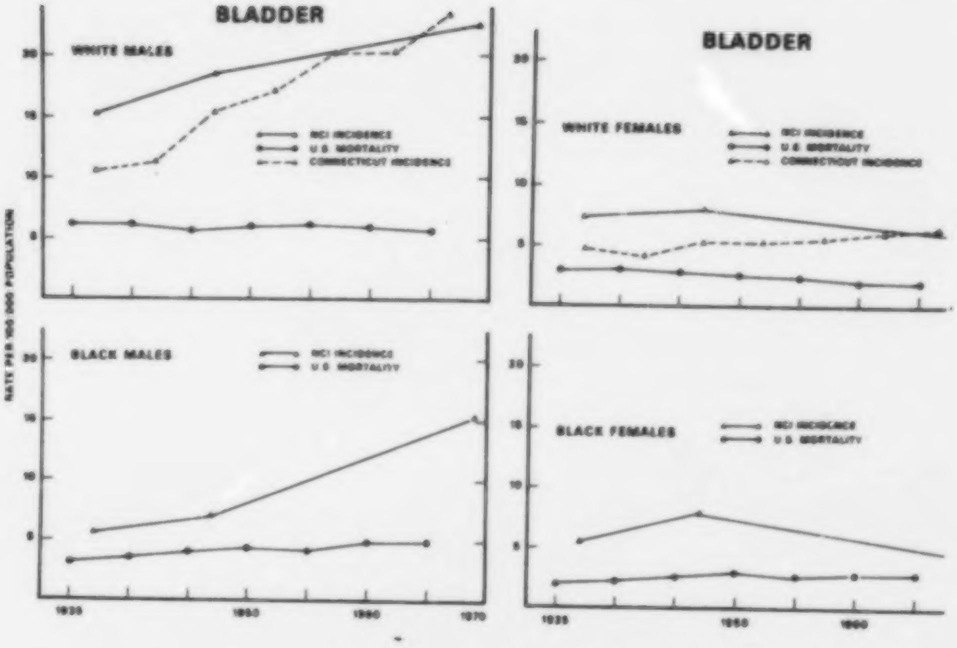

FIGURE 5. BLADDER: TREND OF CANCER INCIDENCE AND MORTALITY RATES, 1935-1969 (AGE-ADJUSTED, 1950 STANDARD POPULATION

For many types of cancer, specific etiologic factors have not yet been clearly identified, but they may well contribute to the pool of environmentally caused cancers. A large group of cancers is related to endocrine factors, which are not environmental per se, although they can be influenced by exogenous factors, including intake of hormonal preparations.

Cancers are known to have widely varying induction times, some ranging up to 30 or more years. The shortest induction times are found in children with acute leukemia and cancers of the brain and nervous system. We need to learn much more about the induction times of specific types of cancer and the factors influencing the growth rate of the developing tumor.

If we do not have adequate data on exposure to carcinogenic agents at the time of exposure, our first lead may come from the induced neoplasms when they are diagnosed clinically. The SEER Program will provide measures of increased cancer occurrence in specific subgroups of the population. These leads can then be followed retrospectively to determine the causative factors and hopefully prevent further occurrence of the disease.

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ENVIRONMENTAL IMPACT OF CHEMICALS

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ABSTRACT

The early assessment of the impact of chemical products on the environment is of vital importance to the chemical industry. Most programs in existence in the chemical industry for evaluating the environmental impact of products depend upon laboratory testing and, based on the results of those tests, the subsequent prediction of environmental behavior.

Laboratory tests begin with a determination of basic physical, chemical and biological properties of the specific chemicals contained in the product. Depending on the results of the simple tests and the anticipated uses and production volumes, more sophisticated evaluations may be required. The environmental behavior of a chemical is predicted in terms of its lifetime, movement, bioconcentration potential, and spectrum of biological activity. Appropriate guidelines for handling, use and ultimate disposal of the products are drawn from the assessment of environmental behavior.

The validity of the early assessment is constantly monitored by actual observation of the effects of chemicals in the real environment. This is done both by monitoring the health of people exposed to chemicals, and by monitoring the environment around the manufacturing plant.

INTRODUCTION

A few years ago the Council on Environmental Quality reported that there were about 9,000 synthetic organic chemicals in commerce. Most of them are used in very small quantities, but a significant number are major products that play a vital role in our society. Virtually every product now used by man is in some way impacted by one or more of these chemicals. Since many of these compounds are foreign to the biosphere, the development of techniques for predicting and evaluating potential harmful effects caused by their release to the environment is of great value to society. For this reason, I welcome the opportunity to discuss the program in effect in my company which I believe is effective in attaining the goals of an early warning system for toxic substances.

METHOD OF EVALUATING IMPACT OF CHEMICALS

I am going to discuss how we evaluate the environmental impact of chemicals by describing procedures followed during the development of a new product. While many industrial chemicals were introduced into the marketplace before environmental testing became part of product development, the principles and laboratory test methods described can be applied to them equally well. My message is that the impact of a chemical on the environment can be predicted from the results of suitable laboratory tests. The testing program, coupled with appropriate use of chemicals, is our most powerful tool for environmental protection. The function of additional early warning systems should be to back up and plug the gaps in the predictive testing program.

The development process for a new chemical usually goes through four distinct stages. The first is the inventive or conceptual stage in which the compound is synthesized and partially characterized. The chemical formula molecular structure and a few basic properties are determined. Depending on a variety of factors beyond the scope of this discussion, the chemical may or may not be further developed as a useful product.

In Stage Two a new compound is further characterized and general use categories are defined. During this period we begin the evaluation of the environmental impact of the chemical. We have found four key parameters are helpful in evaluating that impact, namely, stability, movement, bioconcentration and toxicity.

Stability

The stability of a molecule under conditions encountered in nature has a direct bearing on its impact on the biosphere. The measurement of thermodynamic properties related to stability using classical techniques, for example, calorimetry, differential thermal analysis, along with flash points and flammability limits are helpful in assessing handling hazards. However, for the assessment of environmental impact it is more important to answer the question, is there a mechanism by which the chemical will be removed from the environment under natural conditions? Once the route or routes for removal are established, measurements relating to the rate of decomposition are made, and this data coupled with other information described below, leads to an estimate of lifetime and steady state concentrations in the environment.

Pertinent laboratory measurements are the rates of hydrolysis and oxidation of a molecule. The results of such measurements can be judiciously transferred directly to the environment. Perhaps the most important route of degradation of organic chemicals in nature is microbial metabolism. The classical measurement of oxygen uptake by microorganisms as a result of their action on a test chemical is relatively inexpensive, and provides useful data for estimating the lifetime of a molecule in aquatic or soil environments. If a molecule degrades rapidly to materials already in the environmental sink as indicated by these basic tests of hydrolysis, oxidation and microbial decay, the probability of long-term problems arising as a result of its use is greatly diminished. Of course, if the degradation generates other compounds equally foreign to the biosphere, it is necessary to evaluate the environmental impact of those compounds as well.

Movement

The second key parameter for evaluation is movement. Movement encompasses release to the environment and the various pathways followed after release. If a molecule moves widely, its potential for having an adverse effect may be greatly enhanced. Conversely, rapid dispersion in the environment often results in dilution to levels of no practical concern. Once the chemical enters the environment, a knowledge of its vapor pressure and water solubility provide a basis for estimating transport within the biosphere. For example, if a molecule is volatile, stable, and relatively non-polar it will enter the atmosphere and movement will be rapid and widespread. Polar molecules tend to be more water soluble, and are more likely to move with water. This information is vital when considering which degradation routes will be most important. These measurements are simple to make in the laboratory but translation of the results to a quantitative prediction of movement in the environment is difficult. Comparison of laboratory data on test chemicals with that obtained on compounds whose movement in the environment has been at least partially determined is of value in making predictions.

Bioconcentration

In addition to movement with air, water and soil, a compound may enter living organisms and move throughout the complicated web of biological life. It is, therefore, necessary to analyze the third area for concern; namely, bioconcentration. Laboratory methods for measuring bioconcentration or predicting its likelihood have been used widely only in very recent years. The bioconcentration mechanism believed to be operative for organic compounds is the preferential solubility of the material in fat as compared to water. Since the fat phase of the biosphere is largely present in biological tissue, materials with high fat solubility and low water solubility are likely to undergo bioconcentration. Thus, a good qualitative indication of bioconcentration potential may be obtained simply by comparison of the solubility of a compound in water with that in non-polar organic solvents. For a more quantitative assessment, the partition coefficient, arbitrarily defined as the amount of a chemical dissolved in octanol divided by the amount dissolved in water in a system containing the chemical in equilibrium with the two phases, is usually taken as a good indicator of bioconcentration potential. The partition coefficient can be measured or calculated using the method of Leo, Hansch and Elkins.(1) Recently, experiments by Neely, Branson and Blau(2) show that a good correlation exists between measured or calculated partition coefficients and the observed bioconcentration of non-metabolized chemicals in rainbow trout. It appears the bioconcentration potential of a chemical in the environment can be predicted with reasonable accuracy if its partition coefficient, movement, and stability are known.

Toxicity

The fourth key parameter that must be evaluated is toxicity or more broadly speaking, biological activity. The initial toxicological testing of Dow products is done in-house using a series of relatively inexpensive range finding tests. These include evaluation of toxicity to plants, microorganisms, aquatic organisms, birds and insects.

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(2) W. Neely, D. Branson, and G. Blau, to be published.

Testing on mammalian species includes administration via ingestion, inhalation, skin and eyes. The testing is not extensive at this stage and is designed to determine the effects of acute exposure only. However, when coupled with the information described earlier in terms of bioconcentration, stability, and movement, and also with some knowledge of the effects of chemicals with similar properties on living organisms, a pretty good indication can be obtained of the overall biological effects of the chemical.

Thus, at this stage of development the environmental impact of a chemical can be assessed with some degree of certainty. The basic measurements have been vapor pressure, solubility in water and organic solvents, partition coefficient (calculated or measured), biological oxygen demand, reactivity with water and oxygen, and acute toxicological range finding tests.

It might be useful to consider an example. Table 1 shows the data that would be obtained in Stage 2 on three chemicals with widely differing properties. Based on this information one might predict the following: Perchloroethylene would tend to move mostly in the atmosphere and would have only a very slight tendency to bioconcentrate. The preliminary data indicates a need to further investigate the persistence of perchloroethylene as commercial development proceeds. Hexachlorobenzene appears to be stable and would tend to bioconcentrate. Without doing further work, we would predict it could be a problem if released broadly to the environment in large quantities. Propylene glycol would tend to move with water and be rapidly biodegraded. No environmental problems are anticipated with its use unless a massive release at one location occurs.

A significant comment may be offered at this point. Environmental impact should always be judged on the basis of the combination of all four key parameters, i.e., stability, movement, bioconcentration and toxicological activity. They are strongly interrelated. For example, it is possible for a material to be stable and persist for a long time, but if it is something like concrete or glass and remains confined or has very low toxicity, it is not likely to constitute an environmental problem. Another example relates to bioconcentration. It is often assumed that if a compound has a high potential for bioconcentration it automatically has the potential for severe environmental damage. However, bioconcentration is not likely to be a problem if the molecule is unstable and has a low environmental lifetime. Bioconcentration is a reversible process, and as long as ambient levels are low because decomposition is fairly rapid, build-up in living tissue is not likely to be significant.

TABLE 1. STAGE TWO EVALUATION OF ENVIRONMENTAL PROPERTIES

	Perchloroethylene	Hexachlorobenzene	Propylene Glycol
Vapor Pressure, mm Hg at 20 C	13	10^{-5}	0.2
Water Sol. ppm at 25 C	150	.035	00
Partition Coefficient Calculated, Log	2.26	6.3	-0.8
Bioconcentration Factor in Trout[(a)]	40	8,500	<1
BOD_5, % of theoretical	0	0	70
Reactivity			
Water	Slow	Stable	Stable
Oxygen	Slow	Stable	Stable
Acute Toxicity	Low	Low	Low

(a) W. Neely, D. Branson, and G. Blau, to be published.

Stage Three of product development is often called the pilot plant stage. It usually involves manufacture of the material in developmental quantities, providing necessary information from which to design a production plant. In addition, the proposed application of the material is usually fairly well defined and serious efficacy testing is undertaken. Environmental impact is also evaluated in more depth during this period of development. The testing required depends on the intended use of the chemical and the results of the environmental impact assessment made during Stage Two. For example, in terms of stability, if it has been observed that a molecule would be readily degraded by action of microorganisms or through reaction with water or oxygen, and the molecule is water soluble and likely to migrate to the water phase in the environment, ambient levels of the chemical will remain low precluding widespread environmental problems. Very little additional information would be needed in the evaluation of stability during Stage Three. However, if no route for exit from the environment is apparent, more detailed studies may be necessary. Possibilities include evaluation of photochemical decomposition or studies on metabolism by plants and animals.

Environmental movement may be further evaluated by measurement of adsorption on solids, migration in soil and the transport across the water/air interface. Movement in a closed laboratory ecosystem may also be observed. These techniques have been used in the study of pesticides, but their use has not been extensive for industrial chemicals.

Additional toxicity testing may also be required at this stage. The type of studies necessary depends on an evaluation of the extent of exposure of various types of biological life to the chemical and the results of the earlier toxicity testing. At this point sufficient mammalian toxicological testing would be conducted to set maximum allowable exposure levels for humans who must handle the chemical during production, transportation and use. While many factors influence the design of a toxicological testing program, one important guideline for applying the results is that the exposure levels, route of entry, and test species used be appropriate for the type of hazard being evaluated. Depending on the physical and chemical properties of the compound and the extent of human exposure anticipated, costs for mammalian toxicological testing may run from several thousand to several hundred thousand dollars per product.

An effective medical surveillance program for the experienced engineers and scientists handling the chemical at the pilot plant stage provides real life experience on safe handling procedures. Analytical methods are also perfected at this time to allow detection of the chemical in question in environmental samples.

Let's go back to our three examples. An investigation of the photodegradation of perchloroethylene showed it to degrade in sunlight with a halflife of the order of two days. Since it would be expected to move in the atmosphere, photodecomposition would be expected to be the most significant route of exit of perchloroethylene from the environment. The rate is fast enough so that problems from environmental buildup would not be anticipated. Sufficient mammalian toxicological work has been done to establish a TLV of 100 ppm for the vapor providing a criterion for safe handling of the chemical by humans. In the case of hexachlorobenzene additional work has been done to show it has a high chronic mammalian toxicity. This, together with its stability and likelihood for bioconcentration, suggests HCB should not be developed for applications where it would be spread broadly in significant quantities in the environment. Propylene glycol has had a considerable amount of additional toxicological investigation primarily to allow its use in food, but the early basic studies had shown it would not persist or bioconcentrate, and therefore, would not likely cause adverse environmental effects.

Stage Four might be characterized as early commercialization of the new product. During this stage production of commercial quantities of the compound is begun. Since the production plant itself is a potential source of discharge of the material to the environment, observations on the environment surrounding the production plant provide a pretty good indication if the initial test data correctly predicted environmental impact. Good industrial hygiene and medical surveillance programs for employees in the production plant give an early warning if potential problems exist that had not been anticipated from mammalian toxicological data and pilot plant operations.

Thus, the evaluation of the environmental impact and safe handling of a chemical by humans involves not only predictive testing in the laboratory carried along at various stages of the development, but also careful observation on the actual environmental impact associated with its manufacture and handling at the production site.

An additional point might be made, particularly with respect to chemicals already in commerce. Laboratory data of the type described earlier, together with appropriate environmental parameters, may be used to calculate the rate constant for removal of the chemical from various parts of the environment. If one can estimate the rate of input of the chemical, and if steady state conditions are assumed, the concentration of the chemical in that part of the environment can be calculated. Comparison of the expected steady state concentration with the appropriate toxicity threshold gives an estimate of the margin of safety associated with that rate of input of the chemical. A few measurements of ambient levels serve to indicate if steady state conditions have been reached or if environmental buildup is still occurring. I think this type of analysis is of value, especially in the context of early warning systems for environmental monitoring.

As I indicated earlier, this presentation has been structured within the framework of product development. It also reflects the approach and point of view of at least one major chemical company. Programs similar to this one are the primary device to protect both humans and the environment in general from adverse effects caused by environmental exposure to products of high technology. I believe such programs are effective. However, no program is perfect and they all suffer from dependency on human judgment and understanding. Therefore, the development and incorporation of additional practical, meaningful Early Warning Systems into our society that can supplement existing protective programs without inhibiting innovation is certainly a worthy objective.

ENVIRONMENTAL STRESSOR MATRIX SYSTEM FOR EARLY WARNING

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INTRODUCTION

Early identification of toxic substances continues to be a pressing problem facing mankind. Despite diligence on the part of industry and government, toxicants are introduced into man's environment from a variety of sources. The need for an early warning system has been well established in the previous papers presented at this conference. It is clear that any early warning system must consist of several interconnected elements - Surveillance leading to hazard identification: Continuous surveillance of toxicants within commerce, other warning centers (e.g., poison control), scientific literature especially toxicology, and technical meetings. Assessment of the nature and severity of the hazard: Qualitative linking of potential cause and effect relationships by recognized toxicologists, and quantitative modeling efforts to estimate magnitude of problem and select best control options. Action by decision makers: Agency or agencies to select and control actions.

Through two prior studies(1, 2) for the Department of Health, Education, and Welfare, Battelle has examined the subject of early warning systems and has developed a concept for a system. The system deals with environmental stressors which are defined as the environmental agents or factors of concern reduced to their simplest terms or their most fundamental unit. Examples of environmental stressors and hierarchical patterns are presented in Table 1. Under a current contract for the Office of Toxic Substances of the Environmental Protection Agency, Battelle is further studying and evaluating methods for toxic substance identification. The results of the current study were dicussed earlier in the session by T. J. Thomas and J. E. Flinn. This paper is addressed to the use of of an environmental stressor matrix as an early warning concept which was evolved during the previous studies.

TABLE 1. EXAMPLES OF ENVIRONMENTAL STRESSORS

- CHEMICAL
    - Organic Compounds
        - Ketones
            - Methylbutyl ketone
            - Methylisobutyl ketone
        - Aromatic compounds
            - Polychlorinated biphenyls
    - Silicon, Germanium, Tin, Lead, and Compounds
        - Halides of Ge, Sn, Pb
        - Oxides of Ge, Sn, Pb
    - Pesticides
        - DDT (including its isomers and dehydrochlorination products)
        - 2,4,5-T
- BIOLOGICAL
    - Allergens
        - Inhalants
        - Foods
    - Infectious Microorganisms
        - Bacteria
            - Salmonella
            - Viruses
- PHYSICAL
    - Noise
    - Radiation

SURVEILLANCE – HAZARD IDENTIFICATION

The major categories of information needs of an early warning system have been identified as(3):

(1) Primary production data
  (a) Description of processes
  (b) Number and location of plants
  (c) Annual production records
  (d) Distribution and use categories

(2) Secondary product formulation
  (a) Description of processes
  (b) Number and location of plants
  (c) Capacities and production by end product

(3) End-product distribution and use
  (a) Historical records
  (b) Current annual use data
  (c) Identity and properties of most important formulations
  (d) Industry forecasts

(4) Environmental contamination
  (a) Geographical distribution
  (b) Distribution between soil, water, air, and life
  (c) Movement in the atmosphere

(5) Toxicological manifestations
  (a) Physiological interaction with man
  (b) Toxicity level
  (c) Symptomatology
  (d) Epidemiology.

A means to organize and present this information in a form that can be used as part of an early warning system is an environmental stressor matrix. The concept of the stressor matrix borrows heavily from ideas developed by Lee(4) and Isard(5), and upon the use of input-output techniques in the mental health field by Hutchison and Krause(6). One of the objectives of the use of the environmental stressor matrix is to trace an agent from its several sources along all of its environmental pathways through various receptors to determine its effect upon man. The environmental stressor matrix arrays stressors against sources, transport paths, and effects classifications. The matrix effectively connects the early warning concepts embodied in surveillance of commercial trends with toxicological responses. If quantitative information can be obtained, the stressor matrix can provide much of the needed information for mathematical modeling.

The environmental stressor matrix concept is illustrated in Figure 1. The breakdown of the classifications under each of the columns of the matrix is listed in Table 2. Each row in the matrix is headed by an environmental stressor (Table 1). In the second column, sources (the amount of the stressor released to the environment from a given source) are tabulated. Convenient units for the information in this column could be quantity (mass, number, decibels, etc.) per unit time or quantity per unit activity in the economic sense. The third column of the matrix, medium, represents an instantaneous distribution of the stressor among the media indicated. The values in this column could be expressed in terms of amount per unit volume, area, or mass appropriate to the stressor. There should be a mass balance between all of the second and third columns. At this point, it appears convenient to separate the stressor matrix

		TRANSPORT PATH						
Stressor	Sources	Medium		Compartment	Portal of Entry	Target (Site) of Action	Population Subgroup Modifiers	Consequences
	Quantity per unit time or Quantity per unit activity	Concentration	HUMAN	Exposure per unit time	Quantity per unit activity	Concentration per unit exposure		
				Compartment	Target of Action		Group Modifier	Consequences
			BIOTA	Exposure per unit time	Concentration per unit exposure		Factor	

FIGURE 1. PRELIMINARY ENVIRONMENTAL STRESSOR MATRIX CONCEPT

TABLE 2. BREAKDOWN OF COLUMN CLASSIFICATIONS

Sources

Use standard industrial classifications. Major divisions given below.

- Agriculture, Forestry, and Fisheries
- Mining
- Contract Construction
- Manufacturing
- Transportation, Communication, Electric, Gas, and Sanitary Services
- Wholesale and Retail Trade
- Finance, Insurance, and Real Estate Services

Medium

Atmosphere
Hydrosphere
Lithosphere
Biota
Humans

Compartment - Humans

Domestic
Occupational
Service
Recreational
Transportational

Portal of Entry

Skin
Respiratory tract
Alimentary tract
Genito-urinary tract
Sensory apparatus

Target (Site) of Action

Total organism
Systems
Organs
Tissues
Cells
- Chromosomes
- Organelles
- Membranes

Population Subgroup Modifiers - Humans

Genetic
Group patterns
Individual experience
Physiological status

Consequences - Humans

Physiological-psychological
Longevity
Productivity
Metabolism
- Reproduction
- Normality

Economic
Political
Sociological

Compartment - Biota

Producers
Herbivores
Carnivores
Detritivores

Targets of Action - Biota

Biome
Ecosystem
Community
Population
Organism

Group Modifier - Biota

Consequences - Biota

Longevity
Productivity
Reproduction
Normality

into two parts, one dealing with humans and the other treating the biota. In the next column in the humans section of the matrix, compartment, the exposure to the stressor per unit time (and, if convenient, unit concentration) is tabulated. This column effectively partitions the exposure according to individual activities. Under the portal of entry column, data on the stressor are tabulated, by amounts, in the various pathways. The target site of action is identified, and the concentration of the stressor in the target for a given unit of exposure is tabulated. Population subgroup modifiers are factors that should be applied against sensitive population subgroups. The amplification factor and the sensitive group must be tabulated. Under the consequences column, the effects or consequences of exposure to a given stressor are presented. In the biota section of the matrix, it appears desirable to have different column headings, perhaps amount accumulated per unit mass, within the classifications of producers, consumers, and detritus. The target for the impact of the stressor are the biome, ecosystem, community, population, or organism; and if there are modifiers, they should be noted.

The environmental stressor matrix provides a framework for following the stressor through the environment, and the quantitative data will serve as input to predictive mathematical models. By inspection of the matrix, the significant sources of the stressor and principal elements along its transport path can be identified. This information in itself is useful to suggest means to minimize or eliminate the consequences of a stressor in the environment. If attention is directed to one of the columns of the matrix, the possibilities for synergistic or antagonistic effects exists. Data should be evaluated in light of these possibilities.

Each column of the matrix provides a means for hazard identification. For example, the first column, sources, relates directly to the first of three information needs noted previously. A detailed examination of primary production data, secondary product formulation, and end-product distribution and use can serve to identify if there is a loss of the product to the environment.

For example, in the study of the environmental hazards of mercury(1), an examination of the use pattern for 1965 indicated how mercury was added to the environment. The electrolytic preparation of chlorine and caustic soda had required large quantities of mercury. It was estimated that, by 1970, about 16,000 flasks* would be consumed annually in the electrolytic production of chlorine. This amounts to about 44 flasks (3,300 lb) per day, and could be a source of contamination for water and for air. Agriculture, including its use of fungicides, herbicides, and insecticides, added about 250,000 lb of mercury to soil, water, and the air. About 575,000 lb of phenyl mercurials, mildew-proofing materials for paints, found their way into the air, streams, and the soil. Antifouling agents in paints accounted for about 20,000 lb of mercury in the air, streams, and soil. Through the use of phenyl mercurials by the paper industry, about 45,000 lb per year of mercury were added to the waters. Through the burning of paper, some of this entered the atmosphere. The use of approximately 250,000 lb of mercury in pharmaceuticals, especially as diuretics and anti-infectives, led to direct contamination of man with mercury and subsequent addition to waters and the atmosphere. The preparation of catalysts required approximately 75,000 lb of mercury that found their way into air, water, and probably soil. Likewise, amalgamation led to about 37,000 lb of mercury for release to soils and waters. About 125,000 lb of mercury were used in dental preparations. Some of this probably became an environmental hazard.

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*A flask = 76 pounds.

To illustrate further the applicability of the environmental stressor matrix concept, the available data for the lead(7) and pesticide(8) case studies were summarized and are presented in matrix form in Table 3. Only a single line entry for the source information was made for each of the stressors, and the quantity of the stressor produced annually is indicated by the parenthesis. A more complete representation of the source information would be a two-dimensional array showing the transfers of the stressors between industries. For illustrative purposes, only a few categories under the transport paths are shown and the data are limited to humans.

An examination of the use pattern for 1969 and the immediate years preceding indicates how lead is added to the environment. Although there have been fluctuations in quantities in the use categories reported, no major changes in the categories themselves have been reported during the last decade. That is, the major uses of lead during 1969 continued to be (in decreasing order) in the production of storage batteries and accessories, gasoline antiknock additives (mostly tetraethyllead), red lead and litharge pigments, ammunition, solder, cable covering, and calking lead. An inspection of the materials requirements and manufacturing processes for the lead-acid storage batteries, e.g., preparation of pasted plates, preparation and assembly of grids, and particle size distribution and grinding of

TABLE 3. ENVIRONMENTAL STRESSOR MATRIX – PRELIMINARY

Stressor	Source (Standard Industrial Classification)								
	Agricultural Production 01	Forestry 07	Metal Mining 10	Construction, Special Trade Contractors 17	Ordnance and Accessories 19	Chemicals and Allied Products 28	Primary Metal Industries 33	Fabricated Metal Products 34	Electrical Machinery 36
					Tons				
Lead			(501, 886)(a)	112, 256	[illegible]7, 805	373, 014	(1, 539, 757)(b, c)	211, 681	558, 121
DDT	16, 770(d)	3, 747(d)				(67, 897)(d)			

	Medium			Compartment			Portal of Entry		
	Air, μg/m³	Water, μg/1	Land, μg/g	Domestic, μg/m³	Occupational, μg/m³	Transportational, μg/m³	Skin, μg/day	Respiratory Tract, μg/day	Alimentary Tract, μg/day
Lead	1.6 to 4.0 (urban)(e)	1.5 to 60.0 (drinking)(f)	13.9 to 95.7(f)		1.0 - 49.0(e)	0.1 - 3.5 (alkyl lead)(e)	Negligible	20.0(f)	300.0(f)
	0.5 (composite rural U.S.)(g)								
					1.0 - 11.0(e) (insecticides)	1.3 - 2.8 (inorganic)(e)			
DDT	1 x 10^{-4} (total U.S. average)	0.02 (drinking)		0.0005	0.01 - 0.04				40.0

TABLE 3 . (Continued)

	Target (Site of Action)		Consequences	
	System, µg/100 g	Tissues (Autopsy Tissue),(g) µg/100 g	Acute	Chronic
Lead	Blood 17	Bone (flat) 210-1110 Bone (long) 670, 3600 Liver 120 Kidney 50 Muscle 80 Spleen 30 Lung 20 Ash Adrenal 53 Liver 150 Aorta 160 Lungs 67 Cecum 38 Pancreas 69 Kidney 120 Trachea 58 Larynx 95	TEL penetration of skin: Insomnia, headache, restlessness, dizziness, irritability, ataxia, delusions, anemia, and sometimes convulsions Ingestion of metabolic lead: Pain, leg cramps, muscle weakness, paresthesias, depression, coma, death	Anorexia, a metallic taste, constipation and severe abdominal cramps, pallor, elevated blood pressure, wrist drop, foot drop, encephalopathy
DDT		Body Fat 2.4 - 3.7 ppm(b)	Mild cases Headaches, dizziness, gastrointestinal disturbances, numbness, and weakness of extremities, apprehension, and hyperirritability Large doses Muscular tremors, convulsions, cardiac or respiratory failure, and death	

(a) Mine production of recoverable lead in 1969.

(b) Total new supply of U. S. lead in 1969.

(c) Total consumption based on SIC categories; estimated undistributed consumption 42,300 tons. 1969 use consumption pattern gives 42,000 tons undistributed consumptior (Mineral Industry Surveys. Lead Industry – Preliminary Totals for 1970, U. S. Department of Interior, Bureau of Mines.)

(d) Frear, D. E. H., "Pesticide Handbook-Entoma", Twenty-First Edition (1969), p 28 (Pesticide Usage, 1964).

(e) Symposium on Environmental Lead Contamination, December 13-15, 1965, PHS Publication No. 1440 (March, 1966).

(f) Haley, T. J., Air Quality Monograph No. 69-7, American Petroleum Institute, N. Y. (1969).

(g) U. S. Public Health Service, Survey of Lead in the Atmosphere of Three Urban Communities, Publication No. 999-AP-12 (January, 1965).

(h) Hayes, W. J., "Monitoring Food and People for Pesticide Control", in Scientific Aspects of Pest Control, Publication 1402, National Academy of Sciences – National Research Council, Washington, D. C. (1966).

lead oxides revealed cases of lead intoxication in 66 battery-based industries in Pennsylvania. The use of old battery cases for fuel and resulting lead-containing ash also were identified as environmental hazards of air and soil.

Examination of the use pattern of leaded gasoline additives tetraethyllead (TEL) and lesser amounts of tetramethyllead (TML) indicated that leaded fuels continue to be a major source of environmental lead. Each gallon of today's gasoline contains on the average of 2 to 3 grams of lead (maximum of 4 grams), which adds up to approximately 540 million pounds of lead consumed, according to gasoline sales. An estimated two-thirds of the lead exits through the exhaust, and about half of the exhausted lead becomes airborne, that is, each year about 180 million pounds of lead swirls into the atmosphere. Analysis of atmospheric precipitation samples of lead and other metals collected by a nationwide network of 32 stations throughout the United States indicated that the concentration of lead in precipitation correlated with the amount of gasoline consumed in the area in which the sample was collected. The above two investigations suggest that leaded gasolines contribute notably to the environmental (soil and water) burden. Red lead and litharge-based paints were identified as an environmental hazard during shipscrapping because of the high temperatures involved in burning off (volatilizing) the spent paint.

ASSESSMENT - VERIFICATION

Qualitative-Pollution Chain Diagrams

Once a potential environmental hazard is identified, it is important to determine the nature and extent of the hazard and to verify that cause and effect relationships exist. A pollution chain diagram which graphically presents the environmental flow of the stressor from its sources to its receptors is useful. Examples of pollution chain diagrams for lead and DDT are shown in Figures 2 and 3. These diagrams can be used for a qualitative assessment of potential hazard or can be used as the basis of a mathematical or quantitative evaluation.

For example, there is little indication of lead accumulation in foods, and the concentration of lead in drinking water is relatively

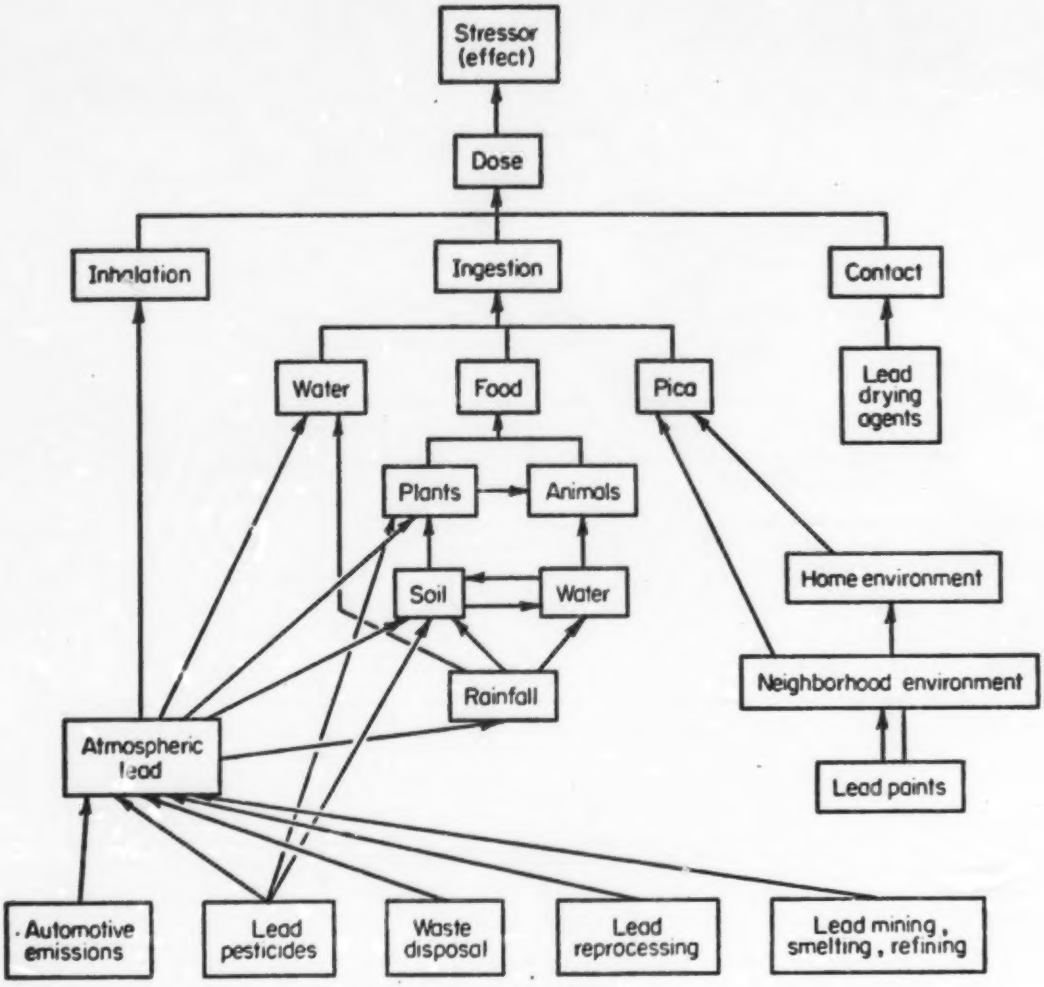
Stressor (effect)
Dose
Inhalation
Ingestion
Contact
Water
Food
Pica
Lead drying agents
Plants
Animals
Soil
Water
Home environment
Rainfall
Neighborhood environment
Atmospheric lead
Lead paints
Automotive emissions
Lead pesticides
Waste disposal
Lead reprocessing
Lead mining, smelting, refining

FIGURE 2. POLLUTION CHAIN DIAGRAM FOR THE ENVIRONMENTAL STRESSOR LEAD

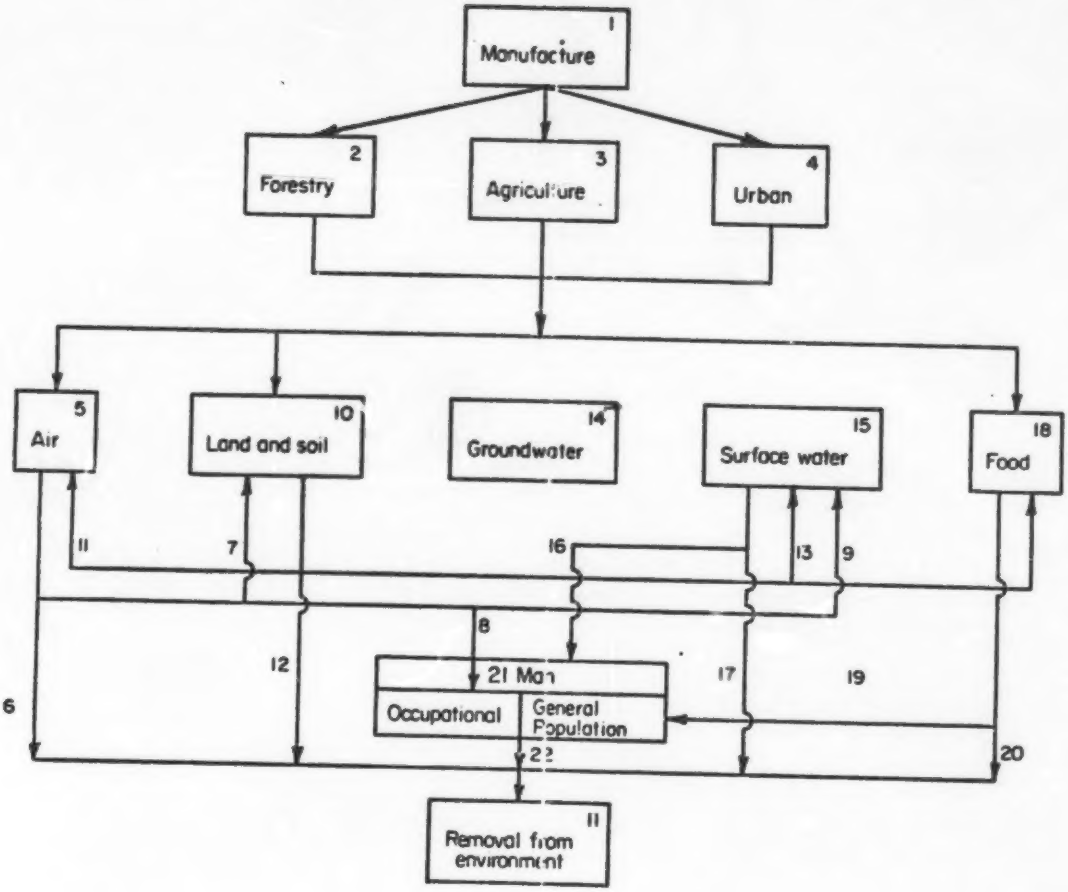
Manufacture
1
Forestry
2
Agriculture
3
Urban
4
Air
5
Land and soil
10
Groundwater
14
Surface water
15
Food
18
11
7
16
13
9
8
12
6
17
19
21 Man
Occupational
General Population
22
20
Removal from environment
11

FIGURE 3. CRITICAL PATHS OF DDT IN THE ENVIRONMENT

Code	Component OP Process Description	DDT Concentration, degradation rate
1	DDT used in U. S. in 1964	18.14×10^{6} kg
2	DDT used in Forestry in 1964	3.40×10^{6} kg
3	DDT used in Agriculture in 1964	9.53×10^{6} kg
4	DDT used in Urban area in 1964	5.22×10^{6} kg
5	Amount of DDT in atmosphere over U. S. at one time	3.6×10^{5} g
6	Half life (T1/2) of DDT in atmosphere	30 days
7	Deposition rate of DDT in atmosphere (1964)	3.86×10^{-7} g/m^{2}/year
8	Inhalation of DDT from atmosphere	
	(a) In heavily sprayed areas	0.0002 to 0.0008 mg/man/day
	(b) In large cities	0.000009 mg/man/day
9	Deposition rate of DDT in atmosphere (1964)	3.86×10^{-7} g/m^{2}/year
10	DDT applied to soil system in 1964	12.93×10^{6} kg
11	Rate of injection of DDT in atmosphere over U. S. (1964)	3.0×10^{6} g/year
12	T1/2 of DDT in Soil System	3.0 years
13	Annual DDT in runoff	2.86×10^{5} kg
14	DDT in ground water	Insignificant
15	Amount of DDT that reached estuaries and ocean from U. S. in 1964	2.63×10^{4} kg/yr
16	DDT intake from drinking water	0.000023 mg/man/day
17	Degradation of DDT aerbic water	$T1/2 = 5.0 \times 10^{-2}$
18	Total DDT in foodstuffs	Data unavailable
19	DDT intake from food	0.04 mg/man/day
20	DDT metabolized by general population	Data unavailable
21	DDT consumption general population	0.09 mg/man/day
22	DDT loss from body storage	<0.3%/day

low. By inference, then, the primary ingestion path for lead is through pica with the source being lead paints. The effect – the observation of high lead levels in children from urban substandard housing areas – can readily be related to one major cause. Since the use of lead as a pigment for indoor paints has been banned, the environmental hazard is localized. The obvious corrective action is to locate and remove lead-based paints from ghetto houses.

Similarly, cause and effect relationships can be discerned for the potential human hazards from DDT in the environment. Two major pathways were considered. Figures 3 and 4 summarize the observations. The first, the direct pathway, deals with the direct uptake from primary sources of pesticide release. Primary sources were manufacture and application. Human exposure was by inhalation. Dermal uptake and ingestion are secondary features. Accidental poisonings remained about the same, even though the frequency of application and the acute toxicity of the new pesticides has increased. These trends suggest that a very credible job of education is being done at the industrial level. Since most of the victims of death from accidental poisoning were children, further reductions could be made by reduction of the total toxicant contents of the home package to below the child lethal dose, where possible, and elimination of those chemicals that cannot be used within the safety margin (e.g., substitution of carbamates and pyrethrians for organophosphate insecticides). Prescription and dispensing pesiticides by trained professionals would also reduce accidental deaths. Aerial application accounts for the largest number of deaths and either elimination or control of this method appears worth study.

The second pathway, the indirect pathway, involves human exposure by translocation through the air, water, or food. While more complicated to consider and model, the indirect pathway involves the total biosphere. The general population of the United States is exposed by this means. Serious conflicts exist in the data as to which indirect pathway leads to the major store of pesticides in man. On a worldwide basis, the persistent pesticide content of man is remarkably constant. Within the United States there are, however, significant racial and geographic differences. Such differences are difficult to explain if food is the major transport pathway to man. The southern population and the southern Negro have greater levels of pesticides than the northern equivalent populations. On the basis of this, together with some indirect evidence from residues in animals, it is likely that only 50 percent of the body burden is from food; the remainder may come from inhalation of insecticide aerosols or dust laden with insecticides. If these observations are correct, then control of the human burden of pesticides by control of food residues, as is now practiced, is at best only partially effective.

Quantitative – Mathematical Models

The environmental stressor matrix provides a means to summarize pertinent data for a quantitative assessment of the magnitude of an environmental problem. In its most general sense, the integrated exposure to man from an environmental stressor can be represented as:

$$E_{ijk} = \int_{t_1}^{t_2} S_{ik}(t)\, P_{jk}(t)\, D_i(t)\, dt,$$

where E_{ijk} is the exposure from stressor i over time t_1 to t_2 through pathway j to man at location k_1

S_{ik} is the time varying source strength of stressor i at location k,

P_{jk} is the "pathway term" for pathway j and location k, and

D_i is the exposure commitment rate for stressor i.

A stressor-environment-man relationship has to be determined to represent the chemical, physical, and biological processes that are elements of the terms S_{ik}, P_{jk}, and D_i. The pollution chain diagram can be used as the basis for developing the quantitative relationships involved. A mathematical model was developed from the pollution chain diagram for lead (Figure 2) to predict blood lead levels due to the intake of lead by ingestion and inhalation. The schematic representation of the model for lead in the body is shown in Figure 5. Literature data on intercompartmental transfer coefficients (e.g., elimination rates) were used in the model and predicted blood lead levels resulting from ingestion and exhalation were compared with measured values. The estimates from the mathematical model were similar in magnitude to the measured blood lead levels.

Several exercises were performed with model to determine the nature of potential hazards and to estimate the effectiveness of

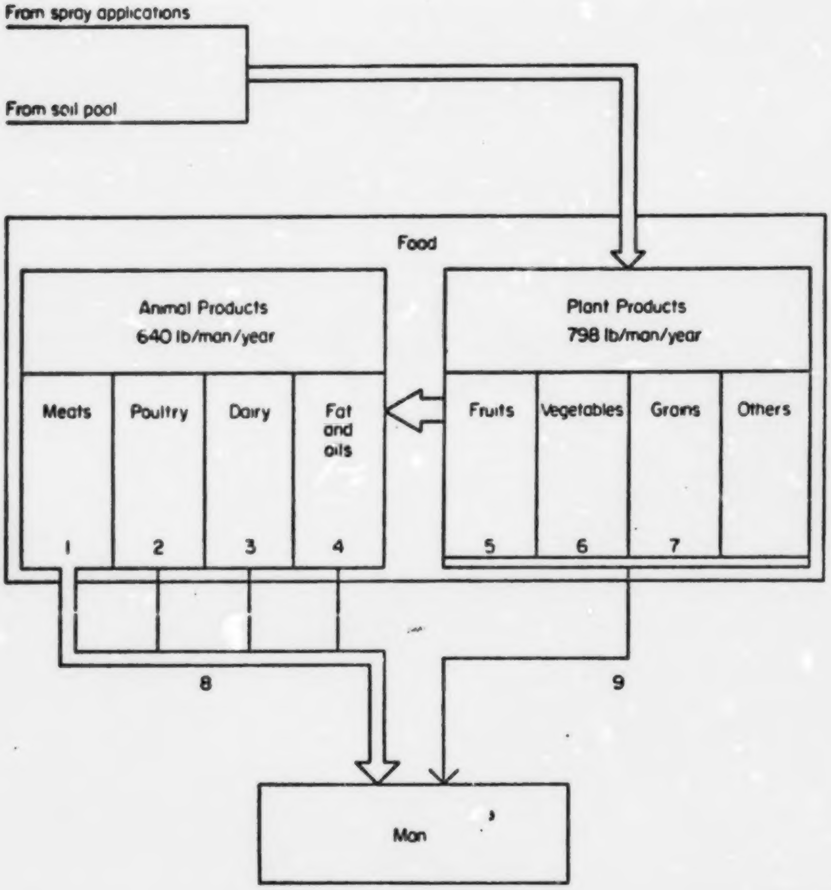
From spray applications
From soil pool
Food
Animal Products
640 lb/man/year
Plant Products
798 lb/man/year
Meats
Poultry
Dairy
Fat and oils
Fruits
Vegetables
Grains
Others
1
2
3
4
5
6
7
8
9
Man

FIGURE 4. CRITICAL PATHWAY FOR DDT TO MAN THROUGH THE DIETARY PATTERNS OF THE GENERAL POPULATION

1. Total intake of meats and meat products was 157.7 lb/man/yr.
2. Total intake of poultry was 87.7 lb/man/yr.
3. Total intake of dairy products was 364 lb/man/yr.
4. Total intake of fats and oils was 51.3 lb/man/yr.
5. Total intake of fruits was 132.1 lb/man/yr.
6. Total intake of vegetables was 199.9 lb/man/yr.
7. Total intake of grains was 35.7 lb/man/yr.
8. DDT intake attributed to meat and meat products was 0.31 mg/man/day.
9. DDT intake attributed to plant products was 0.04 mg/man/day.

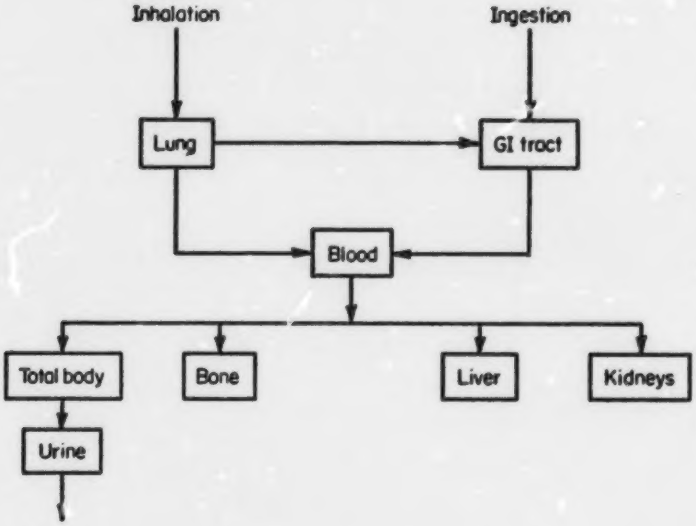

FIGURE 5. LEAD IN BODY MODEL

possible control strategies. Figure 6 shows blood lead-level concentrations as a result of removing lead from the air. The long-term blood lead levels are controlled by the continuous daily ingestion of lead in foods (300 mg Pb per day). In the case of an individual chronically ingesting more lead than the average intake, e.g., ingesting 1000 mg of lead daily instead of 300 mg, and residing in a city location where he is inhaling airborne lead at a concentration of 1.0 mg/m^3, the blood lead concentration would rise to a new equilibrium value of approximately 54 mg/100 g blood as shown in Figure 7. Blood lead levels approaching 50 mg/100 g of blood warrant therapy in order to avoid the central nervous system syndrome of adult or pediatric plumbism. Since a few small chips of paint prior to the lead pigment ban may contain 100 mg of lead, control of lead ingestion by a young child having pica to an intake of less than 1000 mg/day is obviously a difficult task. A substantial improvement in the environment is required.

ACTION .

The previously described elements of the environmental stressor matrix system are passive elements, i.e., they represent the

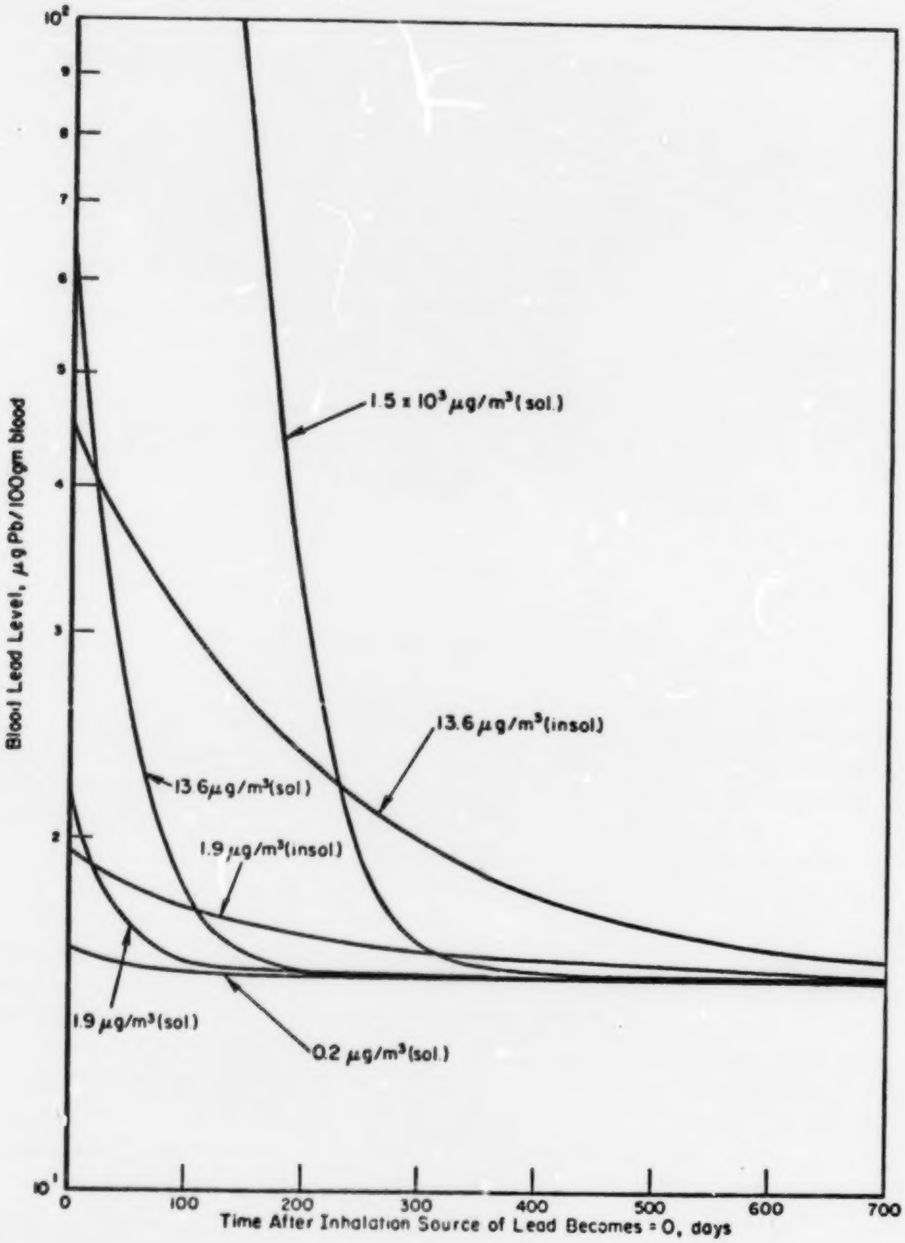

FIGURE 6. BLOOD LEAD CONCENTRATIONS AS A RESULT OF REMOVING LEAD FROM AIR

At time = 0, blood lead level due to continuous daily ingestion of 300 µg Pb per day and inhalation of airborne lead as indicated on each curve.

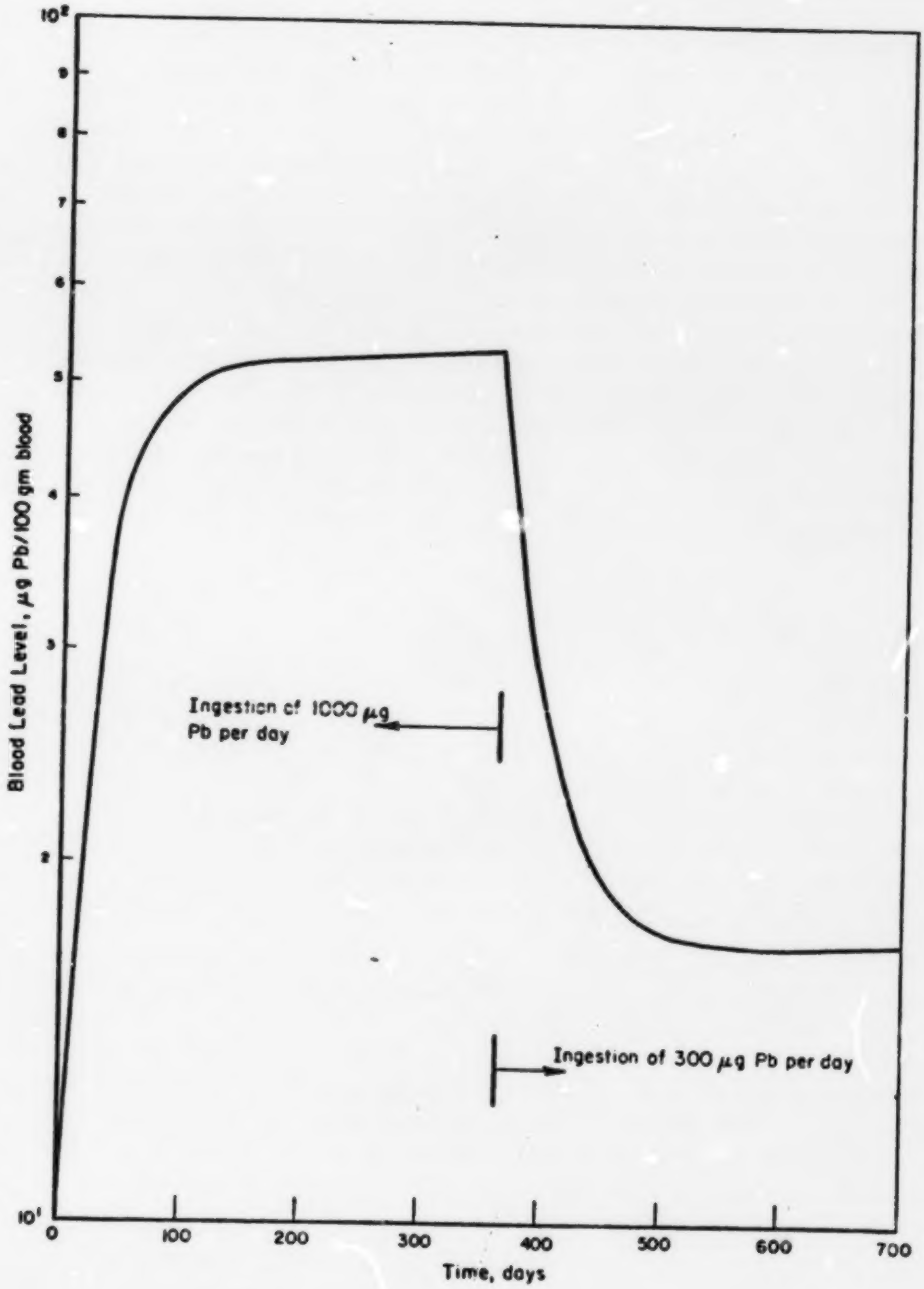

FIGURE 7. CHRONIC LEAD EXPOSURE

Constant inhalation of 1 µg Pb/m^3.

identification and collection of data and information upon which subsequent actions are to be taken. The final element of any early warning system must include several options for actions. Potential environmental hazards once they are identified must be drawn to the attention of some decision maker. The means to do this must be forceful and direct enough to attract the decision maker's attention but must not prematurely raise alarm among public sectors. Opportunities must exist for corrective action to be taken by industry or other sources without severe economic or operational penalties. A detailed discussion of action systems are beyond the scope of this paper. It is essential, however, that such systems must include a multiplicity of disciplines to provide an evaluation of the potential hazards, and government as well as industrial decision makers to affect the required actions. The two elements of the environmental stressor matrix system, surveillance and assessment described previously, can be adapted to fit the needs of any action system.

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PUBLIC INTEREST METHODS FOR ASSESSING CHEMICAL HAZARDS

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INTRODUCTION

We have evolved an early warning system for detecting and assessing chemical hazards. While our resources are limited, our numbers small and our methodology simple, still we are determined to continue to show proper scientific concern about the vast explosion of chemicals inundating our society. We have never taken the time to totally evaluate the success of our efforts, but CSPI has kept in constant touch with the mass media and we have goaded regulatory agencies into taking many of our projects seriously.

GENERAL REMARKS

While speaking mainly of CSPI activities I must admit that there is a strong and growing current of cooperation among a number of public interest, community, environmental, consumer and labor groups. We're all limited in resources and so such cooperation is necessary. Thus environmental legal groups such as Environmental Defense Fund and Natural Resources Defense Council work with us on asbestos and gasoline additive problems. We work with Consumer's Union on Aerosols, with Concern Inc. on lead problems, with Health Research Group on talcs, and with the Urban Environment Conference on air pollution problems. Actually in the course of a year we join forces with 30 some groups on major problems. So important is this aspect of our work that we sponsor through a Meyer Foundation grant a project called "Professionals in the Public Interest" which matches volunteer scientists and economists with citizen groups desiring professional assistance on their projects. The most recent activity is the publication of "Public Interest Letter" which is a monthly report addressed to those who wish to apply their skills to social action projects.

Second only to group and individual cooperative endeavors in importance is that of accessibility to the general public. People must know who we are, that we are credible and that we are willing to listen to their concerns. Many Americans are desirous of becoming more socially concerned, but while being scientific experts, they do not know the art of getting their concerns before the proper authority. They need to be assured that their findings be held in confidence. They need encouragement in whistle-blowing.

A third factor worth considering is credibility. In order to be believed we have to cultivate the mass media, for it can make or break our final story. We must foster an active voluntarism in both resource personnel and in funding sources (usually limited to small donors and foundations). We must acquire a certain number of successes for the track record is always needed for credibility.

From the public interest staff standpoint, a certain flexibility is paramount. We must continue to circulate, to attend scientific and technical meetings, to consult, to talk to technical people in industry and researchers in universities and to build up a system of advisors with whom we can consult on CSPI policies.

Flexibility is preserved if our system is not totally "systematic". A pre-alert system which is overly systematized is simply not workable enough to be fully effective. If bureaucrats construct it then it's most likely too cumbersome. For what we are on the lookout for is precisely the unsystematic in our society, and that can only be partly found through systematic plodding and investigation.

The complementarity of the systematic and the nonsystematic, of art and science, and of intuition and logic, has been known since the dawn of philosophical thought.[*] Signalling an alert to a problem includes an awareness of an unsystematic happening, a recognition that it can be systematically assessed, and the intuitive skills of making the initial findings public. Man's activities are both systematic and nonsystematic. When they are exclusively one or the other there is trouble. An overly systematic person may work to maximize profits on a substance and tend to overlook its potentially harmful effects. On the other hand, one not fully in tune with that particular system can ask the critical question which leads to the discovery of a harmful material.

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[*] For more on this subject of epistemology read B. J. Lonergan's Insight, A Study of Human Understanding.

PROCEDURES

Initial Screening

An accessible, cooperative, credible and highly flexible public interest center can be hindered by a flood of comments, tips, articles and complaints. About half can be either dismissed or routed to other groups immediately for investigation. A certain intuition can divide the others into possible problems and more highly probable problems. In the first category more information would be required from the one giving the first alarm. The motivation of the whistle-blower may vary from the sincere technical expert to the washed out worker who wants a face-saving reason for terminating a job or getting even with someone. He may have found an unusually high incidence of a rare disease traceable to a toxic substance or he may be a kook.

Three techniques for initial review are possible: actual contact with the whistle-blower, or, if that is impossible, a written or phoned request for additional information; inquiry into the credibility of the person; review in confidence of the subject matter presented. Next, samples and/or procedures where required should be submitted to independent laboratories for analyses. This, however, can become quite expensive for public interest groups. Both the lab results and materials submitted by the whistle-blower should be presented to advisors for general comments. They have saved CSPI much time and added efforts.

Assembling Material for Evaluation

Once the initial screening is completed the available evidence must be weighed. This includes answering as many questions as possible about the amount of a material produced or distributed, the number of persons exposed, the seriousness of the suspected malady, the anticipated increase in use of substance, the type of regulation required and - most importantly from a political viewpoint - what alternatives exist which can be easily substituted without unduly disrupting our national economy. Face it, economics pulls more weight on Capitol Hill than does health.

In Washington human resources are available for a proper assessment: willing experts in governmental agencies; offices of professional and trade associations; private foundations and even a host of experienced retirees willing to investigate problems. Also there are many libraries as those at NIH, the Departments of Agriculture, Commerce, Interior, the Library of Congress plus the American Chemical Society library and a number of good specialized sources of information such as the American Petroleum Institute or the Chemical Manufacturers' Association.

Once the data is collected we attempt to assemble the relevant materials in a report, which is not a final document but a blueprint for action on a particular problem. The report passes through the hands of about a half dozen reviewers who have a variety of technical skills and backgrounds. Generally we prefer face to face confrontations with the critics so that the remarks are fully understood. We try to do this before the final touches are on the report to prevent personal bias of the writer from standing in the way of critical evaluation.

The Alert is Sounded

With the report on the toxic substance accepted, we then begin to enter a most critical stage: the presentation of the matter to the public. Here several alternatives should be weighed. It might be better to work quietly within governmental agencies if there is some degree of success promised by responsible people there. It might be best to blast the findings across the wire services and TV networks. This tactic may seem jarring to you because it goes counter to the scientific practice of never saying anything until everyone knows for certain. Incidentally, social action is the only practice among scientists which demands certainty; even their research findings can be quite uncertain if they get them published.

The type of activity should not be limited to mere publicity or threat of legal action. Actual teaming with pro bono lawyers and discussing the matter is important as well as examining the possibility of testifying at appropriate congressional committees, organizing citizen groups to lobby for needed legislation and regulations, and formation of coalitions of citizen groups to apply the proper pressure for action. We recommend a holistic approach of trying to get several courses of action undertaken simultaneously. Such can be done by mapping out the many places where a contaminating substance is used and which regulations exist for curbing it.

Specific Examples

Here are three examples of where a prealert warning method has been applied:

(1) Toxic Substance Understood but Use Overlooked CSPI has been working on asbestos problems for about two years and our research associate, Barry Castleman, has facilitated research by independent laboratories. We found that asbestos is present in alcoholic beverages through the use of filters made from asbestos. We examined a number of sources of drinking water which was carried through asbestos cement pipe and found fibers in drinking water. This was confirmed by an earlier Johns-Manville report. We have taken a number of steps beyond writing an asbestos report (Asbestos and You): joint action with EDF prodding FDA to ban use of asbestos filters and talcs in foods, drugs and drinks; petition to FTC to place propert warnings on asbestos products; and a petition to the EPA to prohibit the use of asbestos cement pipe for drinking water. All of this is part of a prealert on a well-known carcinogenic material in product lines which have been overlooked.

(2) Allied Chemicals to Known Toxic Ones We have been working on gasoline additives for a number of years. A number of the additives listed are quite harmful to people, but these have been overlooked due to the toxicity of gasoline itself. We are particularly alarmed about such materials as TCP (especially in oil) and Ethyl's manganese gasoline antiknock which might become more popular if lead is successfully phased out.

(3) Toxic Substances Previously Overlooked In a recent report "How Aerosols can Affect your Safety and Health", we have tried to present a summary of the toxic effects of various household aerosol sprays. We raised the question of increasingly numerous incidents of misuse. Hazards can arise from exposure to the freon propellants and active ingredients, use in close quarters, failure to read labels and follow directions, propensity for abuse by adolescents, and availability to small children. A number of aerosols can more

easily lead to trouble such as the caustic oven cleaners and air fresheners. Our report caused the Consumer Product Safety Commission to call for the first public hearing of the Agency later this month.

There are a number of other issues which have been examined and acted upon. Some point to immediate alerts and some such as our fluorides study show no need for alarm. We admit that the method of alerting will be subject to fuller development, but we are confident that a public interest element will be needed for some time to encourage proper monitoring of our use of chemicals.